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CARDIOVASCULAR AND CARDIOPULMONARY EMERGENCIES AS SEEN BY AN ANESTHESIOLOGIST *

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Circulatory failure, pulmonary edema, bronchospasm and cardiac arrest — these are some of the clinical pictures imprinted in the mind of the anesthesiologist. He has learned to anticipate these emergencies, even during simple operative procedures in patients with normal cardiovascular and respiratory systems. He is trained and prepared to diagnose these emergencies when they arise and handle them with a cool head, swiftly and competently without losing time. However, his main thought is **to prevent** their occurrence. In order to do this, he needs the cooperation of the patient's physician, the internist, the cardiologist, and the surgeon. Intelligent evaluation of the patient's cardiac and pulmonary status before undertaking a surgical act, and the best possible correction of any accompanying disease are necessary in order to obtain an uneventful operation.

Adequate preoperative sedation of the patient, careful selection and administration of the anesthetic, provisions for maintaining clear airways, avoidance of hypoxia and hypercapnia, and provisions for offsetting the deleterious effects of harmful positions and unavoidable reflexes are some of the prime obligations of the anesthesiologist to his patient. Moreover, blood loss must be replaced under his direction without overloading the circulation. Any change in the color of the patient or in the rate and rhythm of the heart should be noticed and evaluated immediately, so that the necessary correction can be instituted at once.

The Preoperative Period

The principles of preoperative evaluation and preparation include the knowledge that:

a) a hypovolemic patient is poorly equipped to tolerate blood loss during surgery;
b) anemic patients are unable to tolerate hypoxia or blood loss; and,
c) it may be difficult to recognize hypoxia when it does occur in such cases.

If heart failure has been present in a patient it should be corrected before instituting a surgical procedure. Even rapid digitalization may be indicated in the last few hours prior to surgery, if necessary. A complete evaluation of the cardiac condition should be available to the anesthetist in cases where hypertension, rheumatic valvular disease, coronary heart disease or conduction disturbances are present in addition to the condition which brings the patient to surgery.

If hypotensive drugs or steroids have been administered to the patient in the past, information about dosage and time of administration should be available.

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Hypertensive patients who have previously been given hypotensive drugs may exhibit a severe drop in blood pressure during anesthesia, especially when spinal anesthesia is administered. Patients who have received steroid drugs for any length of time, even many months prior to surgery, or patients with chronic disease who may have developed adrenal insufficiency may have to be prepared and maintained before, during, and after surgery with adrenal corticoid therapy, so that they may withstand the stress of the operation.

A suspicion of glaucoma in any patient should be communicated to the anesthetist, so that both atropine in the preoperative sedation and succinylcholine during anesthesia can be avoided, in order not to increase intraocular pressure.

Adequate preoperative assurance to a frightened patient, together with preoperative sedation, prevents high adrenalin output that might otherwise sensitize the myocardium of the patient to some of the current anesthetic agents or might produce a severe increase in the work of the heart.

Administration of alkaloids of belladonna is important preoperatively (a) to decrease secretions and thus make it easier to maintain a free airway, and (b) to decrease vagal reflexes that may arise during intubation or surgery.

The stomach should be empty in every patient undergoing **elective surgery,** and no food should be given within eight hours preoperatively. In **emergency surgery,** the stomach may have to be emptied with a stomach tube; otherwise, an endotracheal tube with a cuff may be introduced into the trachea and the cuff inflated while the patient is awake in order to prevent aspiration. This is the method of choice in patients with a bleeding gastric ulcer or bowel obstruction. If possible, patients should be brought out of shock before starting any anesthetic procedure, and electrolyte balance should be restored.

The Operative Period

In order to make a wise **choice of the anesthetic procedure,** the anesthetist, in addition to knowledge of all the above factors, should be familiar with all anesthetic agents and procedures at his disposal. Some anesthetics are parasympathomimetic drugs which may cause laryngospasm and bronchospasm (thiobarbiturates and cyclopropane), while others are sympathomimetic (ether). Likewise there are anesthetic agents which may interfere with the cardiac rhythm, have a toxic effect on the myocardium, or lower the blood pressure. Each of these agents and methods may be safely used if given cautiously and with proper attention to detail. If general anesthesia is selected as the anesthetic of choice, obstruction of the airways should be avoided at all cost. Endotracheal intubation should be used when the patient is in the prone or an unusual position, in upper abdominal surgery, and in chest and brain surgery. In order to prevent hypercapnia, the breathing of the patient should be assisted. Controlled respiration may interfere with the venous return to the heart, whereas assisted respiration does not cause such interference.

Hypercapnia is recognized as one of the major factors in enhancing the effect of vagal stimulation on the heart. Sudden cardiac arrest due to **vagal** stimulation, e.g., due to spreading the ribs, rarely occurs without the presence of hypercapnia. Unless the anesthesiologist pays special attention, hypercapnia may not be easily recognized because the patient's color is pink, especially if a high oxygen concentration is used in the anesthetic mixture. This is illustrated by the so-called "cyclopropane shock," which is recognized as a post-hypercapnic phenomena[1]. At the end of the operation, when fresh air is inhaled and the accumulated CO_2 is exhaled, the blood pressure suddenly drops, the pulse slows down, and the patient exhibits a shock-like appearance.

However, hypercapnia can be prevented if adequate ventilation has been supplied during anesthesia by assisting the respiration of the patient. As the medullary center is depressed by the anesthetic agent, and the respiratory muscles are partially paralyzed by the use of relaxing drugs such as succinylcholine or curare, it is obvious that, in order to avoid hypercapnia, constant

assistance to breathing is necessary to assure adequate ventilation.

The exact physiological mechanism of cardiac arrest is poorly understood, but Miller and his associates have shown in animal experiments that the sudden return of elevated carbon dioxide to normal levels can produce ventricular fibrillation and death[2]. Wiggers[3] submitted dogs to inhalation of carbon dioxide and demonstrated a prolongation of the conduction time when the blood pH was lowered. Campbell and associates[4] have shown that inhalation of CO_2 increases the cardiac response to vagal stimulation, and Young et al[5] have found that hypercapnia, and not hypoxia, enhances the effect of vagal stimulation of the heart. Therefore, it can be assumed that, by preventing hypercapnia during anesthesia, we can protect the patient against the danger of vagal stimuli causing cardiac arrest. Thus, hypercapnia should be avoided at all cost. A rise in blood pressure or an increase in pulse rate, possible signs of initial hypercapnia, should be investigated at once. A sudden fall in blood pressure and slowing of the pulse rate call for immediate action, i.e., increased ventilation, administration of atropine, and stopping the surgeon from continuing maneuvers which cause the reflex action until normal conditions are resumed. Such incidences are quite frequent in upper abdominal surgery. It should also be noted that acidosis due to disturbances of the electrolyte balance will enhance the effect of a vagal stimulus just as much as hypercapnia.

Sloan[6], in a series of animal experiments, was unable to produce even temporary cardiac arrest in dogs exposed to normal concentrations of oxygen. Temoprary cardiac arrest occurred, on the other hand, during a condition of hypoxia, but more frequently during hypoxia plus hypercapnia. In clinical anesthesia, any respiratory obstruction may produce hypoxia or hypercapnia. It is relatively easy for the experienced anesthetist to avoid **upper respiratory obstruction** by using an endotracheal tube, as pointed out before, but **lower respiratory obstruction** might pose a more difficult problem. Atelectasis may arise and not be recognized at once because the patient is covered by drapes. Likewise, adequate ventilation may be difficult to achieve in a patient with bronchial asthma and emphysema. The following case will serve as an example:

A 63 year old patient came to the hospital for a colon resection because of carcinoma of the transverse colon. He suffered from bronchial asthma and chronic emphysema and had, in addition to these conditions, infiltration in both bases of the lungs. Cyanosis of the lips was present. The heart was enlarged, and a harsh blowing systolic murmur was heard at the apex in the 6th interspace. A_2 was greater than P_2. Pulse rate was 96 and blood pressure 160/80. The ECG was compatible with coronary insufficiency. The patient received digitalis gr. 1 orally as a maintenance dose on the day prior to surgery and a blood transfusion was started to correct anemia (Hgb. 10.5 gm.) He developed orthopnea after the administration of 100 cc. of blood and increasing dyspnea with the administration of an additional 150 cc.; he also complained of pressure in the chest. The administration of the blood had to be discontinued.

There was subsequently some discussion about the best method of anesthesia. The internist suggested spinal anesthesia. However, since it would of necessity had to have been high spinal anesthesia, and considering the state of the patient's coronary arteries, general anesthesia was agreed upon. Oxybarbiturate was used for induction, succinylcholine for intubation, and small amounts of ether inhalation through an endotracheal tube for maintenance of anesthesia, together with a succinylcholine drip for relaxation. After about an hour of smooth anesthesia, increasing difficulty was noted in inflating the chest. Bronchospasm was recognized, and Benadryl was given i.v. with good effect, followed by a slow drip of aminophylline. In view of the emphysema, it seemed desirable to use a Jefferson ventilator to inflate and deflate the chest, using alternate positive and negative pressures instead of only assisting respiration during inspiration as it had been done previously. No more diffi-

culty was encountered, and the patient made an uneventful recovery.

In other patients, cortisone therapy has been used postoperatively and during surgery to check bronchial asthma. This was effective in a 53 year old patient scheduled for bilateral antro-ethmoidectomy for nasal polyposis which was considered as the focal point for her paroxysmal attacks of dyspnea. The use of thiobarbiturates, on the other hand, is to be avoided in asthmatic patients.

Even slight obstruction of the airway, allowed to continue for some time, may favor pulmonary edema on account of the increased negative pressure necessary to get the air past the obstruction. Patients in whom this condition appears respond favorably to correction of the obstruction and inhalation of oxygen alcohol vapors to disperse the foam.

Interference with oxygenation may be caused by the necessity of subjecting the patient to certain positions, e.g., the Trendelenburg position, which interfere with ventilation and decrease vital capacity. On the other hand, too forceful manual assistance of respiration in a child that is not intubated may cause acute gastric dilation, and the pressure of the gastric fundus on the left diaphragm may in turn interfere with the efficient working of the heart. It is thus possible that, even in the presence of free airways, poor oxygenation of the heart may occur and, if allowed to persist, may lead to cardiac arrest.

Failing of the circulation may occur if there is a rapid and unexpected blood loss; otherwise blood replacement is followed by satisfactory results. No operation should be started without blood available for transfusion, although **plasma expanders** may serve in an emergency. Adrenal cortical insufficiency may be unrecognized preoperatively, as in the case of a 9 year old boy with 3rd degree burns who went into shock during the third operation for grafting in spite of blood transfusions, but responded favorably and instantly to I.V. administration of **Cortef.**

Changes in pulse rate should be recognized and treated at once, and, if necessary, with the help of a continuous E.C.G. Sudden tachycardia and falling blood pressure during surgery may mean hemorrhage; the tachycardia may be a harmless sinus tachycardia, but the E.C.G., on the contrary, may reveal an auricular flutter, at which time rapid digitalization should be instituted. Ventricular extrasystoles occurring during a mitral commissurotomy and recognized by means of the E.C.G. respond favorably to divided doses of quinidine gluconate.

Candidates for mitral commissurotomy should be adequately digitalized before surgery. Tachycardia of 160 on the operating room table in these patients should not be blamed on the preoperative atropine, but on insufficient digitalization. The operation should then be postponed. Other patients develop tachycardia because of the recumbent position which they cannot tolerate.

Fall in blood pressure preoperatively following preoperative sedation should be given full attention. The following case is quite instructive:

A 57 year old patient was scheduled for repair of a right inguinal hernia. The blood count was adequate. The patient's general condition appeared to be good. The preoperative sedation was Phenergan—25 mg., Demerol—50 mg. and Atropine—0.5 mg. He had been admitted on the night prior to the scheduled surgery. His blood pressure upon arrival in the operating room was 80/60 and rose to 100/60 after oxygen administration. An E.C.G. taken the night before had not been read and was hastily sent for; it showed coronary insufficiency compatible with a recent myocardial infarction. The operation was postponed and the patient recovered, as did other patients on whom E.C.G. was done and found to be abnormal after arrival in the operating room, when pulse or blood pressure were not considered adequate and the operation postponed.

The above principles apply to both the preoperative and operative periods. However, it should not be forgotten that the postoperative period is also fraught with danger. Special attention must be paid at this time to the problems of obstruction to the airways (prolapse of the tongue, vomiting, atelectasis, laryngeal edema), inadequate respiratory exchange

(prolonged effects of muscle relaxants, over-sedation, constricting bandages, improper positioning of the patient), fall in blood pressure (cyclopropane shock, internal hemorrhage, inadequate blood replacement) and overloading of the circulatory system with resultant pulmonary edema (too much IV fluids, unrecognized coronary thrombosis during the operation).

The author has attempted to show in the foregoing what to do to avoid cardiovascular emergencies. However, disasters do occur and, in the subsequent paragraphs, it will be shown that one should be prepared for cardiac arrest.

It is common knowledge that time is of absolute importance in resuscitating an arrested heart in order to have the patient recover completely. Four minutes is considered the absolute maximum time allowable for resuscitation. This means that, in a previously well oxygenated patient, there are only four minutes to reestablish the heart beat or institute a facsimile thereof by rhythmic compression of the heart which then supplies a pulse in the periphery and oxygen to the brain.

The lungs should be hyperventilated with oxygen, preferably through an endotracheal tube, in order to provide oxygenation and to avoid the risks of hypercapnia; restoration of the blood volume should likewise be started if this is the cause of the condition. Therefore, no time can be lost in establishing a diagnosis.

Electronic instruments in place during surgery, such as an electrocardioscope, are often of great help in preventing cardiac arrest and should be used more frequently. They are a "must" in all cases of cardiac surgery and during hypothermia, and whenever coronary insufficiency or any other cardiac condition is present, or when considerable stress is expected during surgery. Monitoring devices **in place** at the time of the accident save time in establishing the diagnosis of cardiac arrest or ventricular fibrillation, but no time should be lost in **attaching** a **cardiograph** to establish the diagnosis.

Zoll and his co-workers have described an external pacemaker and an external defibrillator[7] which may be tried if immediately available, thus preventing the necessity for thoracotomy; but here again, time is of the essence, and it should be kept in mind that the pacemaker will not work efficiently in a poorly oxygenated heart though good results seem to occur in patients with Adams-Stokes syndrome so that complete recoveries have been reported.

When no pulse can be felt at the carotid or other large artery, the chest should be opened at once with disregard to aseptic conditions. Ruth[8] was unable to find any patient surviving after cardiac massage who subsequently developed an infection of the chest wall, pleura, or pericardium. Even if the heart is beating slowly and inefficiently after opening the chest, or during chest or heart surgery, massage should be started at once, or the oxygenation of the brain will suffer. Belated massage might restart the heart, but the patient would still not be able to recover from the effects of cerebral damage.

Details about how to open the chest, how to massage efficiently, when and how to defibrillate, and what drugs to use, if any, are commonly available. The following shows how to be really prepared.

Detailed instructions on "what to do in case of cardiac arrest" should be posted in a plainly visible space in every operating room.

A sterile cardiac tray should be available at a moment's notice.

A defibrillator should be ready.

Most important, routine "drills" should be used in order to teach the internes and residents how to use the tray, how to connect and use the defibrillator, and how to massage the heart. In order to educate the internes and residents (and as many physicians as possible), one can repeat Fell's[9] experiment on dogs which shows the increasing anoxia and flabbiness of the heart caused by increasingly obstructed airways until cardiac standstill occurs; then hyperventilation with oxygen and cardiac massage may be started. Moving pictures about cardiac arrest should be also frequently shown.

SUMMARY

It has been shown and illustrated by case histories that cardiovascular and pulmonary emergencies may be anticipated and in most cases prevented by:

(1) Expert preparation of the patient for the operation.

(2) Undivided attention of the anesthetist.

(3) Prevention of hypercapnea and hypoxia.

(4) Watching the fluid and electrolyte balance.

Suggestions are made on how to be prepared for the ultimate emergency once it occurs.

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EMERGENCIES IN ALLERGY †

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Emergencies associated with allergic phenomena are frequently encountered in the every day practice of medicine. Prompt diagnosis, along with a thorough working knowledge of the indications and contra-indications for various medications and therapeutic procedures is essential — since this information or lack of it can produce results ranging from almost immediate relief of symptoms to sudden termination of life. Specific medicaments and equipment should be readily available[18]. On rare occasions where a doubt exists in the physician's mind, (e.g., cardiac asthma, as differentiated from allergic bronchial asthma), treatment should be instituted which would not be harmful to either condition until such time as a definitive diagnosis can be made.

In order to better understand the processes involved in immunologic or hypersensitivity reactions leading to such emergencies in the field of allergy, we shall attempt, at least briefly, to acquaint the reader with some well-established, as well as some of the more recent concepts which have been developed in immunology. Basically, the antigen-antibody interaction is our best fundamental explanation for hypersensitivity[13]. Reintroduction of an antigen into an already sensitized cellular site may produce reaction on the cellular wall in mesenchymal tissue or may involve the mast cell with a concomitant release of histamine. Such sensitivity may occur in the skin, in the mucosal structures of the nose, bronchi, and gastro-intestinal tract, and in other areas; the causative agent is usually a protein, a high molecular weight carbohydrate, or a simple chemical compound, the latter acting as a hapten which unites with a body protein.

Increased knowledge in this field has developed in the past two decades because of the advances in biochemistry, physical chemistry, isotopic nuclear studies, and the unfolding of endocrine actions, especially with reference to the pituitary-adrenal cortex relationship[3]. Such information has become available through the increased usage of the ultracentrifuge, radioactive isotopes, electrophoretic procedures, purification and isolation of endocrine products, and through studies of specific cellular poisons[22].

The antigen in hypersensitivity acts primarily on the reticuloendothelial system, lymphocytes, plasma cells, and on proteins, resulting in an increase of gamma globulin, although the beta globulin may also rise. It is believed that the antigen acts upon undifferentiated mesenchymal cells, or upon plasmablasts, to form a sepcific plasma cell equipped to synthesize a specific antibody directed against the antigen responsible for it. It would follow, therefore, that patients who suffer from agammaglobulinemia would lack the ability to create circulating antibodies. This finding has been proven clinically.

Antigens may be classified according to their source, e.g., inhalant, ingestant, injectant, infectious, and contactant. When any of these reacts with a specific antibody, whether through a proteolytic enzyme system, or more likely in the mesenchymal tissues, especially the mast cell, histamine is released into the surrounding area. The resultant pathologic changes involving localized sensitive cells can be demonstrated clinically as smooth muscle spasm, increased capillary permeability with associated edema caused by diapedesis of fluid through thinned capillary walls and a marked increase in mucous secretions attributable to hyperactivity of the localized mucous glands.

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Acute bronchial spasms, episodes of sneezing with rhinorrhea, and urticaria with or without angioneurotic edema may follow within a few seconds or minutes after antigen-antibody reaction. This we call an "immediate whealing reaction." One must differentiate the "delayed reaction" of the tuberculin or serum sickness disease from the above[8]. Chase[23] has shown that prolonged incubation period is required in the latter variety because the antibody is apparently to be found within the leucocytes. Several days, or even weeks, may elapse before clinical evidence of the delayed type reaction makes its presence known. In this type, edema and tenderness of small joints, often associated with small hemorrhages, together with fever, and in some instances, thrombocytopenic purpura with gastro-intestinal symptoms (Henoch-Schonlein's Disease) may occur. Rich[22] and his colleagues have shown the development of collagen disorders to be a hyperergic response in immunologic processes, caused by foreign sera, bacteria, sulfonamides, and numerous other drugs, and involving the joints, muscles, vascular endothelium, heart valves, kidneys, and other tissues. Infections caused by viruses have recently been included as causes of allergic disorders. The vaccinia virus has been shown to contain a soluble protein antigen, a nucleoprotein antigen, and a hemagglutinin. Hypersensitivity reactions to certain viruses have also been reported, with serious complications in some instances.

The emergency conditions most often encountered, with underlying hypersensitivity factors as a basis, are:

1. Anaphylactic shock.
2. Acute angioneurotic edema.
3. Status asthmaticus.
4. Drug allergy.
5. Serum disease.
6. Thrombocytopenic purpura.

We shall discuss each of these as a separate entity, although fundamentally the reaction involved in each is exactly the same, except insofar as speed of onset and severity. It is our belief that allergy and anaphylaxis are alike, immunologically, except in intensity of the resultant reaction.

1. **Anaphylactic shock**

This condition may follow the use of horse serum preparations in antisera, penicillin by injection as well as orally[4,17], various intracutaneous test materials, not always of high concentration, such as cottonseed[11], egg mustard and others, hormonal extracts such as adrenocorticotropin and insulin, bee and wasp venom[12], orally ingested substances such as cottonseed or various berries, topical application of cocaine and other allied compounds, and the inhalation of certain substances, in concentrated form, as, for example, castor bean dust[9,16].

It is believed that the sudden release of overwhelming amounts of histamine in specific antigen-antibody reaction is responsible for the severity of the reaction. On occasion, an initial contact with one of the above substances may produce the same severe reaction. Accidental intravenous injection may occasionally be a factor, although most reports in the literature, with post-mortem verifications, would tend to deny this. Sudden collapse with weak, thready pulse, stupor, marked pallor, cold sweat, coma, and death may occur within a very few minutes. Accidental intravenous injection of a high dosage of ragweed pollen extract has been known to produce such a reaction as is described above. Following injection of penicillin, there may be strange taste sensations, flushing of the skin, urticaria with or without angioedema, severe dyspnea, dysphagia, involuntary urination and defecation, cyanosis, and severe vertigo as well as other manifestations.

Therapy for this condition must be prompt if the patient's life is to be saved. This requires the presence of an emergency kit, used exclusively for such reactions and replenished as quickly as it is depleted, practically at the physician's fingertips. Modern treatment[7], if the reaction is severe enough to threaten the patient's life, requires immediate intravenous steroid (e.g., sodium succinate ester of hydrocortisone or prednisolone). The former drug is available in a specially prepared vial, in which the dry powder is in one section and the diluent in another, so that pressure on the one

side forces the diluent into the lower chamber, causing rapid solution of the powder and making it immediately available for use. Soluble prednisolone powder (50 mg.) is available in a vial allowing introduction of 2 cc. of sterile distilled water or saline as solvent. This solution becomes immediately available. The recommended initial dosage is rapid intravenous injection of 25 mg.

Other methods which may be employed as adjuvant therapy are:

a. Epinephrine 1:1,000, aqueous, 0.25 to 0.50 cc. subcutaneously, or .10 cc., diluted and given slowly intravenously, or protocatechuyl alcohol hydrochloride, 1 cc. intramuscularly.
b. Intravenous glucose solution.
c. Lowering of the patient's head.
d. Levarterenol bitartrate (or similar preparations), intravenously, using extra caution to avoid leakage into the subcutaneous tissues.
e. Oxygen, by mask, if cyanosis is intensive[19].

Spontaneous recovery may occur in minutes, although some of the above-mentioned measures are usually required. The precaution of pulling back on the syringe plunger before injection of the specific antigen in order to observe entrance of blood into the syringe may help to prevent some reactions. Conjunctival or skin test to a suspect antigenic substance may also help identify such specific sensitivity factors and prevent anaphylactic reaction. A tourniquet applied above an injection site may slow absorption and enable the physician to use any of the above procedures which may be necessary in any given patient.

2. **Acute Angioneurotic Edema**

Acute submucosal and subcutaneous, localized edematous areas may occur within seconds or minutes and threaten life if they involve a vital site. Such is the angioedema which may affect the epiglottis, glottis, trachea, tongue, larynx, or other less vital areas. Often acute generalized urticaria may accompany this condition, although this is much less dangerous since it involves only superficial skin surfaces.

Angioedema may be a part of a drug or food reaction, trauma, infection, or even of unknown origin. Recognition, when it involves the airways, is not too difficult. Evidence of acute, progressive suffocation with cyanosis, caused by anoxemia, is usually easily recognized.

Therapy consists of alleviation of the asphyxial symptoms as rapidly as possible. Tracheotomy may be the most rapid way to get air into the patient's lungs. Any sharp instrument readily available, even a pocket knife, may be used. Because of the critical state of such patients, sterility is ignored until the patient is safely beyond the critical point. Other measures which may be useful, if time permits, include:

a. Epinephrine, parenterally as well as by topical spray or application.
b. Aerosols of any potent sympathomimetic drug.
c. Intravenous hydrocortisone or prednisolone.
d. Intravenous adrenocorticotropin.
e. General supportive measures.

3. **Status Asthmaticus**

Acute episodes of bronchial asthma which persist beyond forty-eight hours, and which no longer respond to repeated injections of epinephrine, subcutaneously — or to intravenous aminophylline, are considered as belonging to the term "status asthmaticus." We feel that such patients are allergic emergencies who could die and are in need of heroic measures — preferably administered in a hospital. Such patients will present symptoms and findings of severe dyspnea, wheezing, varying degrees of pulmonary emphysema, usually accompanied by non-productive cough, at least in the early stages. They may display symptoms of markedly prolonged and labored expirations, severe bronchospasm, hyperresonance due to increase in residual air, restriction of diaphragmatic movement, decrease in maximum breathing capacity, and evidence of hypoxemia with cyanosis. Associated complications may include:

a. Hypochloremia and dehydration due to vomiting or sweating.
b. Cor pulmonale with ultimate right ventricular failure due to gradual increase in resistance in the pulmonary vascular bed with pulmonary arterial hypertension.

c. Chronic progressive pulmonary emphysema, irreversible, with destruction of alveolar septa.
d. Anoxemia and hypercapnia.
e. Severe pulmonary infections with bronchiectasis and accumulations of much mucous and mucopurulent secretions.

Other causes of acute prolonged dyspnea and wheezing must be ruled out including cardiac asthma, tumors (primary and secondary), foreign body, and many others[1,6].

Treatment of status asthmaticus must consider all of the above factors in order to be effective. Since usual dosages of adrenaline and aminophylline seem no longer effective, the following regimen is suggested:

a. Continuous intravenous aminophylline, 1 gm. in 1,000 cc. 5% glucose in saline, at moderate speed, 24 hours per day (NOT in very young children).
b. Sedation, since the patient is usually very apprehensive and has been unable to sleep for two or three days. For all our patients, a "NO MORPHINE" sign is placed on the chart and on the patient's bed. Usually chloral hydrate, paraldehyde, tranquilizers, or other similar preparations will be of some benefit. Demerol, in moderate dosage and given with great care, has been recommended by some authorities.
c. Bronchial relaxants, administered by aerosolization with oxygen pressure, have proved effective in many such cases[10]. Protocatechuyl alcohol hydrochloride (Caytine), 1:100, adrenaline, 1:100, isoproterenol hydrochloride, 1:00 or 1:200, aminophylline solution, either alone or together with desoxyribonuclease (Dornase), or a combination of superinone, sodium bicarbonate and gycerine (Alevaire), and similar preparations have frequently proven to be good adjuvant measures. Isoproterenol sulphate 25% has also been beneficial route and dose.
d. Intermittent positive pressure breathing, with oxygen, administered with great care and watchfulness under capable supervision, has helped in many patients. Oxygen, generally, is contraindicated, except perhaps in severe cyanosis. The reason for this is best explained by the fact that pulmonary oxygen is a more fundamental drive to peripheral and central respiratory chemoreceptors than pulmonary carbon dioxide in acute or chronic hypoxic cases. This primacy of hypoxic control is seen in those patients whose ventilation is so impaired that carbon dioxide accumulates in the circulating blood. These patients are frequently hypoxic and dyspneic. Administration of high oxygen mixtures increases the diffusion of oxygen into the blood stream and abolishes hypoxia, thereby removing the hypoxic respiratory drive and greatly reducing ventilation, thus allowing further accumulation of carbon dioxide. Unless some means of mechanical hyperventilation is provided to remove the carbon dioxide, the abolition of hypoxia in such circumstances may lead to carbon dioxide narcosis and even death.
e. Bronchoscopy and rarely tracheotomy may prove to be life-saving. Removal of an inspissated plug of mucous has been known to open the airway in a bronchus and relieve the acute symptoms. Especially in critically ill children under the age of two years, this may become the treatment of choice. Expectorants, such as potassium iodide, ammonium chloride, apomorphine hydrochloride, and ipecac are useful in helping to liquefy and expectorate excessive mucous secretions.
f. Infections must not be overlooked. Sputa should be examined for bacterial content by direct smears and cultures. Bacterial sensitivity tests to determine the antibiotic of choice should be done soon after the patient's admission to the hospital. Antibiotic aerosols have been employed with good results.
g. Adrencorticotropin and/or steroids, while not to be considered a "last

resort," are nevertheless **not** the "first" drug in our armamentarium. Within twelve to twenty-four hours after the patient's entrance into the hospital, one can usually determine the need for these hormonal drugs. Intravenous ACTH, 20-25 USP units, in 500 cc. of 5% glucose in water, slowly (8-12 hours), daily for three to five days, has been a most effective tool[2]. Its use intramuscularly in gel or suspension is less effective. Usually, on the second or third day of such therapy, oral steroids (cortisone, prednisone, prednisolone, methyl-delta-hydrocortisone, triamcinolone, dexamethasone, or similar compounds) are started, so that when the need for ACTH is gone, the patient has already been on substitution therapy which can be continued at home. The usual precautions must be observed, a salt-poor diet ordered, and additional potassium included. This mode of therapy has yielded the most dramatic results in the relief of status asthmaticus.

4 and 5. **Drug Allergy and Serum Disease**

These already have been referred to, under the heading of "Anaphylaxis."

Since antisera, when used as therapeutic agents[5,21], are actually considered to be drugs, we shall discuss them together.

Symptoms varying from acute anaphylactic shock to mild urticaria may follow administration of oral or injected drugs. Reactions of the "immediate whealing" variety have been dealt with above. The delayed serum sickness disease[8], with its multiple symptomatology, is well known, and while incapacitating, is nevertheless not usually of serious enough import as to require emergent management.

Therapy of the acute reaction requires immediate removal of the causative antigen, as gleaned from a careful history. Prophylactic use of skin and conjunctival tests are advised whenever possible, in order to avoid serious reactions.

The use of epinephrine, ephedrine, and other sympathomimetic drugs usually aids in the relief of the emergency and in the ultimate cessation of symptoms. The antihistaminic drugs are usually of benefit in relief of pruritis, but are of little help in reversing other symptoms of serum sickness. When the above measures fail and the emergency continues to exist, intravenous steroids (as described previously), with or without adrenocorticotropin, usually provide the necessary relief and control of symptoms.

6. **Thrombocytopenic purpura**

Patients may be seen, following exposure to antigen, with evidence of hemorrhage in skin, nose, mouth, gastrointestinal and genito-urinary tracts. Severe secondary anemia may be present, with the patient in a state of shock and collapse, and red blood cell counts and hemaglobin dropping as low as 1,000,000 and 3 gm., respectively.

Use of steroids and epinephrine, as previously described, is indicated along with immediate blood transfusions and other supportive measures.

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THE DIAGNOSIS OF THE DISSEMINATED PULMONARY INFILTRATE

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The problem of differential diagnosis in the patient who is discovered to have a dissemniated pulmonary infiltrate on a chest x-ray is one which clinicians are seeing with increasing frequency. This is in part due to the greater number of such films taken as a routine procedure or in "surveys," and in part to the fact that the chest x-ray has become essential in the approach to any patient with a diagnostic problem.

The case described below is one that presented this problem of differential diagnosis.

Case Report

The patient was a 39 year old Negro housewife who gave a history of having been well until about 3 weeks before admission to the hospital when she started to complain of increasingly severe exertional dyspnea, weakness, and vague substernal pain. She had been unable to fulfill her normal household duties for 10 to 12 days prior to admission. The dyspnea was frequently associated with the chest pain and was gradually relieved after resting 10 to 15 minutes. The chest pain was described as "aching," non-radiating and aggravated by deep breathing. There had been a 20 pound weight loss in the past several weeks (239-219) and the patient had the additional complaint of a mild non-productive cough. Her past history was non-contributory. Arterial hypertension had been noted for the first time during her present illness.

Physical examination revealed an obese Negro female of 39 years, not appearing chronically ill and in no acute distress. The temperature was 98.6° F., the pulse 84 and regular, and the blood pressure readings varied from 150/90 to 200/100. The pertinent physical findings included moderate obesity and diminished breath sounds in the right lower lung field. The heart was not enlarged, A2 was greater than P2 and there were no murmurs. There was no palpable lymphadenopathy or splenomegaly, and the liver did not appear to be enlarged. Exertional dyspnea was easily demonstrable by having the patient walk for less than one minute at a relatively fast pace. During recovery, the patient hyperventilated and complained of dyspnea for an abnormal period of time.

The chest x-ray showed diffuse extensive hazy densities scattered throughout both lung fields with more coalescence in the right middle and lower lung fields. (Fig. 1.) The histoplasmin and 2nd strength PPD skin tests were negative. Sputum studies obtained by bronchial lavage demonstrated no malignant cells, AFB or other pathogens. The serum total protein was 7.4 gm.% with the albumin being 3.8 gm.% and the globulin 3.6 gm.%. The serum calcium was 4.8 mgm.% with the ionized portion being 2.1 mgm.%. The vital capacity was 1.9L and the MBC 82L/min. Arterial oxygen determination at rest was 89% and at recovery, 90.1%.

Bronchoscopy was performed with normal findings, and a biopsy of the bronchial mucosa from the right lower lobe showed normal epithelium. A right scalene fat pad biopsy yielded fibro-fatty tissue. Two weeks after admission an open lung biopsy was performed. Grossly, the lung was indurated and mottled having the consistency of liver tissue. Microscopically, some areas showed an almost complete replacement of lung tissue by non-caseating granulomata compatible with sarcoid. Of particular interest was the finding of granulomata in the bronchial mucosa and in the walls of branches of the pulmonary artery.

On the basis of the histologic evidence of a non-caseating granuloma and the failure to demonstrate any specific etio-

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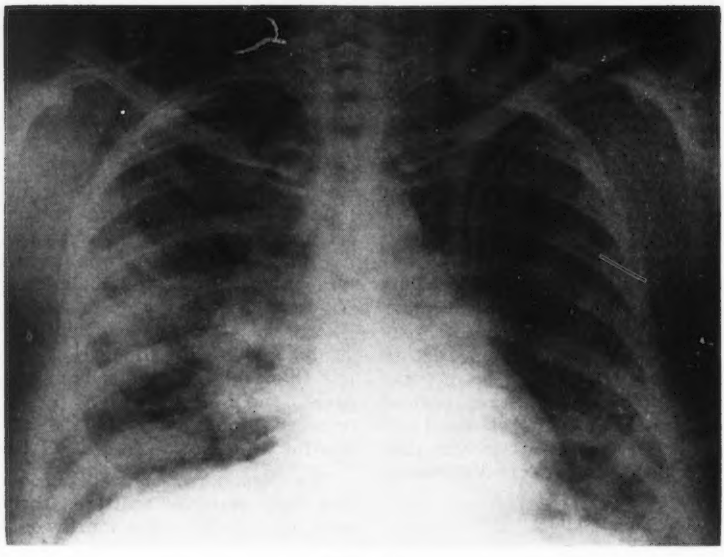


Fig. 1

Diffuse extensive hazy densities scattered throughout both lung fields with more coalescence in the right middle and lower lung fields.

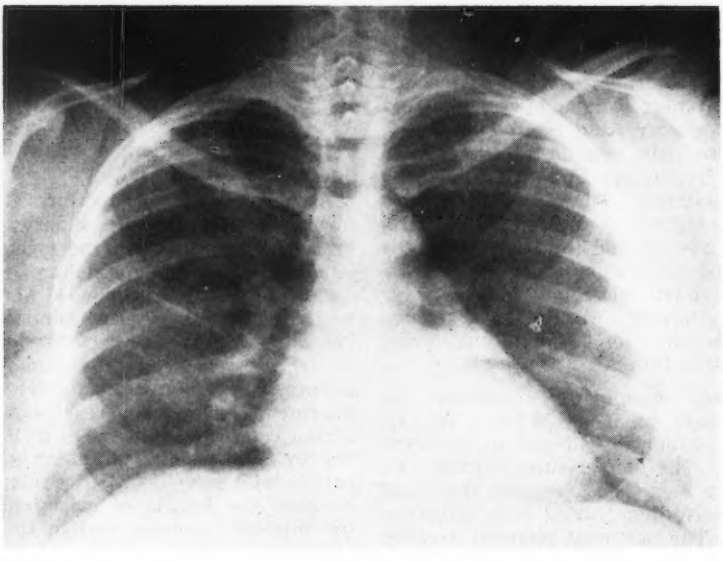


Fig. 2

Complete regression of infiltrate with residual pleural changes in right mid-lung field (post-piopsy).

logic agent, a diagnosis of sarcoidosis seemed warranted. The patient was started on therapy with prednisone in a dose of 40 mgm./day which was then gradually reduced until the patient was able to be maintained on a dose of 7.5 mgm./day. There was dramatic improvement in the chest x-ray (Fig. 2) which showed an almost complete regression of the infiltrate and an equally dramatic improvement in the exercise tolerance without dyspnea that the patient had previously exhibited.

DISCUSSION

Buechner[1] has classified the causes of miliary lung disease as follows:

1. Bacterial disease
- Brucellosis
- Diffuse indolent pulmonary tuberculosis
- Friedlander's pneumonia
- Miliary tuberculosis
- Salmonella infection
- Shigella infection
- Staphylococcal infection
- Tularemia
- Whooping cough

II. Rickettsial diseases
- Q fever
- Rocky Mountain spotted fever

III. **Parasitic diseases**
- Schistomiasis
- Toxoplasmosis

III. Parasitic diseases vapors
- Acetylene gas
- Ammonia
- Bromine
- Carbon tetrachloride
- Chlorine
- Conflagration pneumonia
- Hydrochloric acid
- Hydrogen fluoride
- Lewisite
- Mustard gas
- Nitric acid
- Nitrogen dioxide (Silo Filler's disease)
- Nitrogen oxide (electric welding)
- Phosgene
- Picric acid
- Sulfur dioxide

V. Disorders due to inhalation of foreign materials
- Anthracosis
- Asbestosis
- Bagassosis
- Barium pneumoconiosis
- Beryllosis
- Byssinosis
- Diatomaceous earth disease
- Iodized oil in lungs after bronchography
- Manganese pneumoconiosis
- Osmium pneumoconiosis
- Platinum pneumoconiosis
- Shaver's disease (bauxite)
- Siderosis (arc welder's disease)
- Silver pneumoconiosis
- Soap dust pneumoconiosis
- Stannosis
- Talc pneumoconiosis
- Vanadium pneumoconiosis

VI. Diffuse focal aspiration pneumonia
- After hemoptysis
- After resuscitation from drowning
- Associated with unconsciousness
- Lipoid pneumoria

VII. Allergic diseases
- Asthma
- Hexamethonium and hydralazine intoxication
- Löffler's syndrome
- Tropical eosinophilia

VIII. Fungous diseases
- Actinomycosis
- Aspergillosis
- Blastomycosis
- Coccidioidomycosis
- Cryptococcosis
- Geotrichosis
- Histoplasmosis
- Maple bark disease
- Moniliasis
- Nocardiosis

IX. Viral diseases
- Chickenpox
- Hemorrhagic fever
- Influenza
- Measles
- Primary atypical pneumonia
- Psittacosis

X. Collagen diseases
- Dermatomyositis
- Erythema nodosum
- Lupus erythematosus
- Periarteritis nodosa
- Scleroderma
- Wegner's granulomatosis

XI. Neoplastic diseases
- Alveolar cell carcinoma
- Blood-borne metastasis
- Hodgkin's disease
- Leukemia
- Lymphangitic carcinomatosis
- Pulmonary adenomatosis

XII. Disorders associated with cardiovascular disease
- Hemosiderosis
- Pulmonary edema
- Rheumatic pneumonia

XIII. Spirochetal disease
- Syphilis

XIV. Miscellaneous disorders of uncertain etiology
- Amyloidosis
- Congenital cystic disease with pulmonary fibrosis
- Cystic fibrosis of the pancreas with associated pulmonary fibrosis and infection
- Diffuse bronchiolitis
- Diffuse nonsepcific pulmonary fibrosis
- Eosinophilic granuloma
- Hamman-Rich syndrome
- Hand-Schüller-Christian disease
- Infectious mononucleosis
- Interstitial plasma cell pneumonitis (Pneumocystis carinii)
- Letterer-Siwe disease
- Muscular cirrhosis of the lung
- Mycosis fungoides
- Niemann-Pick disease
- Pulmonary alveolar microlithiasis
- Pulmonary alveolar proteinosis
- Sarcoidosis
- Sickle-cell disease
- Tuberous sclerosis

XV. Disorders of traumatic origin
- Diffuse military hemorrhages of blast injury
- Lightning stroke pulmonary edema

Until recently, the differential diagnosis of the disseminated pulmonary infiltrate was considered as an academic exercise important only in regard to prognosis. During the last decade, however, therapeutic advances have made this view obsolete. These advances include specific antimicrobial therapy for tuberculosis and certain fungous infections, chemotherapeutic agents, hormones and adrenal steroids in various neoplastic diseases, and the use of the adrenal steroids in the non-specific granulomatous diseases such as sarcoidosis and in those believed to be due to a hypersensitivity reaction such as the Hamman-Rich syndrome.

As a consequence of the availability of potent and often specific therapeutic agents which could be hazardous if the correct diagnosis has not been made, it has become imperative to be more exact in our diagnosis of these disseminated lesions. Hence, our diagnostic approach is, of necessity, more aggressive, being satisfied only with accurate histologic, bacteriologic or immunologic evidence of a specific disease.

The investigation of a patient with a disseminated pulmonary infiltrate should include a careful history and physical examination, routine blood and urine studies, blood chemistry determinations, intradermal skin testing for specific granulomatous infections, bacteriologic and cytologic examination of the sputum or bronchial washings, immunologic studies of the patient's serum, bronchoscopy with biopsy of the bronchial mucosa, biopsy of enlarged lymph glands when present or of the scalene lymph nodes when lymphadenopathy is absent, aspiration and culture of bone marrow and needle biopsy of the liver.

When the above procedures are inadequate to establish an accurate diagnosis, lung biopsy is recommended in order to obtain histologic and/or bacteriologic evidence, for an etiologic agent. This is opposed to adopting a policy of "watchful waiting." The method originally advocated by Klassen[2] consisted of a small intercostal incision under local anesthesia and attended with a low morbidity, but the present trend has been toward a more extensive exploratory thoractomy under general anesthesia[3]. The advantages of the latter procedure are that a better selection of biopsy sites is provided, with more adequate exploration of the area, and the opportunity for multiply biopsies is present if indicated.

It should be clearly understood that the diagnostic procedures indicated above, up to and including lung biopsy, are not to be considered routine and ordered as a battery in every case with

a disseminated pulmonary infiltrate. Each patient, as with all patients, is to be considered as an individual problem with the decision as to the extent of investigation being up to the attending physician. Accuracy of diagnosis, however, is the first requirement of proper therapy, so that prior to the institution of potent and possibly hazardous therapeutic agents, it is essential that all diagnostic approaches have been used.

SUMMARY

1. A case which presented as a problem of a disseminated pulmonary infiltrate as shown on x-ray has been described.
2. A diagnosis of sarcoidosis was made in this patient on the basis of histologic evidence obtained by lung biopsy after other diagnostic efforts were unsuccessful.
3. Accurate diagnosis permitted the use of adrenal steroid therapy with excellent roentgenographic and clinical improvement in this patient.
4. A listing of the causes of the problem of disseminated pulmonary infiltrate has been given along with a brief discussion. The need for an aggressive approach to diagnosis has been emphasized in view of the increased availability of specific therapy.

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PSYCHOSOMATIC CONSIDERATIONS OF MASSIVE GASTROINTESTINAL HEMORRHAGE

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In discussing gastrointestinal hemorrhage from a psychosomatic viewpoint, I will include those individuals in whom specific massive gastrointestinal hemorrhage is the basis for seeking medical care. However, the psychosomatic approach compels me to consider not only the complaint of the individual but rather the individual as a whole. This calls for an understanding of:

1) Why gastrointestinal hemorrhage occurs in some individuals and not in others when there are no obvious anatomical and physiological differences between them.

2) The symbolic significance or psycho-social meaning of the hemorrhage for the individual, how he perceives it, his attitude toward the experience, and the probabilities of successful treatment in the light of the total problem seen in its psycho-social as well as physiological dimensions. The psychosomatic approach is directed toward the understanding and treatment of a person with a massive gastrointestinal hemorrhage rather than toward the treatment of a disease, the gastrointestinal hemorrhage.

Attention must be directed first to the influences of the autonomic nervous system on gastrointestinal motility, secretion and vascularity (Necheles and Kirshen),[1] and to the fact that bleeding has been known to occur in many organs of the body as a result of psychic influences. How mental and social actions influence hormonal activity and bleeding from an organ is most dramatically portrayed in the case of the uterus. Menstrual flow can be stopped or started, made more severe or lessened, and menorrhagia and metrorrhagia of such severity as to require transfusion may be initiated by psycho-social phenomena (Kroger).[2] Hemorrhages as a phenomenon associated with life experiences having massive psychic correlates have been described in connection with hysteria as, for example, in the case of stigmata. Hemorrhagic diatheses varying from minor ecchymotic reactions to extensive extravasations in the skin have been described. An entire monograph devoted to this subject is quoted by Dunbar.[4] Hypnosis has been used to decrease or to stimulate bleeding,[5] whichever at the moment may be the desired goal. It should not be too difficult to accept the possibility of hemorrhagic extravasations brought on by psychic stimuli affecting also the gastric mucosa and causing bleeding.

Cases of neurotic reactions associated with gastrointestinal hemorrhage and other gastrointestinal signs and symptoms are cited in the literature. Schindler[6] has shown gastroscopically that transitory parenchymatous hemorrhages occur in the gastric mucosa of neurotic individuals. A possible explanation of massive hemorrhage occurring through psychic stimuli is that of Von Bergman[7] who finds that local ischemia takes place in the muscularis mucosa, followed by self digestion. The experimental work of Wolff and Wolf[8] further documents the evidence of psychic stimuli producing a hyperemic mucosa which can be made to bleed readily by simple irritants.

Psychic factors influencing and predisposing to gastric hemorrhage may function circuitously as well as by direct influence on gastric vascularity, motility and secretion. Cardiospasm induced by emotional problems may be subsequently

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associated with spasm of the pylorus, megacolon and other dysfunctions in the gastrointestinal tract predisposing to hemorrhage. Diffuse hyperplastic gastritis, which may have its origin in a functional disturbance, may lead to peptic ulcers (Taylor).[9]

Peptic ulcers are of course the most common cause of massive gastric hemorrhage. A conflict situation of a specific nature has been suggested by Alexander[10] as the significant etiologic agent: "The wish to remain in a dependent infantile situation—to be loved and cared for—was in conflict with the adult ego's pride and aspiration for independence, accomplishment and self-sufficiency." In essence, the stomach under such conditions behaves as if the person were eating. Secretion and motility continue as if food were ingested, but no food enters the stomach, and the following sequence of events: neuroendocrine system → stimulation → gastric vasoconstriction → gastric hypersecretion → peptic ulcer → erosion of a blood vessel and bleeding. The concept of a specific conflict as the cause of peptic ulcer may not be sustained by further investigations. The case studies on which the hypothesis was formulated were limited in number, and since a control group was not available, it is within the realm of possibility that this type of conflict may be identified in a statistically significant number of people who do not develop peptic ulcer, but some other disease or symptom unrelated to the gastrointestinal tract. It is also possible that a similarly significant number of peptic ulcer patients may not suffer from this type of personality conflict. However, Mittelman and Wolff[11] have demonstrated that normal controls experiencing some acute transitory emotional disturbance as well as patients suffering from ulcer, gastritis and duodenitis showed an increase in the hydrochloric acid, mucous and pepsin secretion. A marked increase in peristalsis was also noted. In the group with organic pathology, these changes were more pronounced. The patients with ulcer reacted more severely with increased pain, increased bile secretion and bleeding.

Acute gastric hemorrhage occurring spontaneously without demonstrable pathology on x-ray, or after surgical exploration is not too uncommon a clinical experience. The significance of acute psychic distress compatible with marked secretory, motility and vascular changes in the stomach has probably been underestimated as a cause for bleeding due to acute ulceration. Spontaneous healing without scarring or other evidence of significant tissue change occurs in the majority of these patients.

Treatment

In a discussion of the concept of diagnosis in medical practice, the model physician-patient relationships have been reviewed by the author.[12] These relationships are determined by the physician's prevailing attitudes towards the patient during treatment, and include the following three models: 1) Activity—Passivity. The patient is relatively a nonparticipant except as the passive recipient of the active interventions planned and executed by the physician; (2) Guidance—Cooperation. The patient seeking help can participate in the activity but sees himself as relinquishing power and authority for decision making to the physician; (3) Mutual Participation. The healer helps the patient to help himself. In the less severe hemorrage, the guidance-cooperation model is more applicable, and in minor hemorrhage, the mutual participation model may be established with the patient. Acute massive hemorrhage, however, is an illness requiring emergency care for a person whose consciousness and ability to cooperate is considerably constricted. The patient, in many instances, cannot even seek help himself and when he can, indicates his state of complete helplessness and his desire to respond passively to the suggested interventions of the physician. Acute illness in general, but hemorrhage of a severe nature in particular, usually mobilizes the need for dependent surrender to authority to a degree beyond that seen in most other illnesses. The patient may be stuporous or semi-conscious; nevertheless, one should avoid saying things in the patient's presence which may increase his

fear and apprehension on the mistaken assumption that the patient does not comprehend what is being said. Not to give every possible reassuring explanation which the patient is able to understand may affect adversely the doctor-patient relationship and impede progress.

Management of the family members is almost as much a part of the treatment of any sudden acute illness as is the treatment of the patient. A calm, deliberate attitude on the part of the physician, reassuring explanations of the nature of the illness, its prognosis, and probable course and the assignment of tasks to keep the members of the family calm or away from the patient may be necessary.

Once the emergency period is over, treatment of the patient requires an awareness of how he has reacted to his illness, his expectations from the physician, and his patterns of dealing with anxiety provoking life situations. Goals for further treatment may then be determined, on the basis of the above considerations, and of the diagnosis of the complex psycho-social as well as biochemical pathology related to the bleeding. In some instances, treatment may require the removal of pathological tissue and surgical repair to achieve the goals of symptom relief, rehabilitation, avoidance of recurrence or exacerbation of the illness, and the slowing or arresting of the disease process. The treatment goals of necessity vary with the total life situation, even when the specific pathology is the same. For instance, conservative management may be considered for a patient fearful of surgery. In others, mild urging may be desirable. On the other hand, a patient who, through religious beliefs, is adamant in his refusal to accept drugs or alter his way of living, may accept a surgical procedure during the immediate period of hemorrhage and may therefore better be considered for early surgical management.

In general, the management of the patient with massive hemorrhage includes:

(1) Dealing with the emergency problem at hand—utilizing those controlling and directing activities necessary for saving life.

(2) A period establishing a guidance-cooperation type of treatment relationship in order to plan further therapeutic goals, such as the removal of pathologic tissue, and the relief of symptoms, after the acute phase of treatment is over.

(3) Special consideration being given to those treatment needs determined by unique factors in each case and aimed at lessening individual, family, and social stresses. For instance, hemorrhage may mobilize feelings related to fears of mutilation, separation anxiety, or longings for security and dependence, and may require reassurance, ventilation, and control of dependency relationships. The specific pathology may require special psychotherapeutic considerations. For example, the patient who has bled from a lesion which is inoperable and which may have a fatal outcome in a short time should be managed with the significant psychologic factors held clearly in mind. Feelings of insecurity may lead to a defensive bravado and a failure to carry out the prescribed treatment. Such a defense may have to be deal twith aggressively. In a patient with hemorrhage from a chronic indurated ulcer for which a surgical procedure is indicated it would be most unwise to destroy such a defense when the hemorrhage will lead to death from an inoperable lesion within a short time.

In short, treatment of massive gastrointestinal hemorrhage, as viewed from a comprehensive concept of medicine, is directed at the total life situation of a patient. There are few conditions more apt to mobilize feelings of extreme apprehension and helplessness in the patient, or to mobilize the physician's desire to be omnipotent and omniscient.

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AN INVESTIGATION OF CERTAIN INTRAPSYCHIC ASPECTS OF DRUG ADDICTION

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During the past few decades interest in the effects of drugs on mental functioning has been of prime import to drug firms, research centers, mental hospitals, physicians in private practice, and mental institutions. In addition to these legitimate centers of interest in drugs, there has flared up, mainly in the large urban centers of our nation, a pattern of illegitimate or illegal drug use that has assumed epidemic proportions.

In noting the longitudinal development of drug use, Bailey[1] stated that:

> "From time immemorial it has been known that chemical substances introduced into the body from outside are able to alter our intellectual and emotional faculties. The effect of ethyl alcohol on Noah is doubtlessly known to you. The **soma** of the ancient Hindus, the **hashish** of the Syrians, and the **peyote** of the Mexicans are other examples. Probably the first scientific study of these pharmaceutical effects was made by Moreau de Tours in 1845. In the report which he made to the Imperial Academy of Medicine he said: 'I saw in **hashish,** or rather in its action on our moral faculties, a powerful means of exploration in the matter of mental pathology; I was persuaded that, by its means, one should be initiated into the mystery of alienation'."

We can note then that drugs which affect mental functioning have been and are used by: (1) medical and allied professions, (2) tribal groups,, usually in conjunction with religious ceremonies, and (3) by individuals with neither of the above determinants. Self-administration is common in the latter two instances. Occasionally drugs that are used in "folk medicine" find their way into legitimate medical use. Such is the case with **Rauwolfia serpentina,** the base of many current tranquilizers, which was used for centuries by women in India to pacify disturbed infants. Contrarywise, such drugs as heroin were first acclaimed for their medicinal value, subsequently abandoned, and are today utilized as the mainstay of the narcotic addict.

"The mystery of alienation" alluded to by Moreau de Tours[2] has itself been the subject of interest and study for a long period of time. The introspective observations in "Confessions of an Opium Eater"[3] have given way to clinical observations[4] and to clinical psychological studies.[5]

It should be noted that one valuable source of information regarding the intrapsychic phenomena associated with drug taking is the anthropologist. Mooney,[6] in his observations of the Kiowa use of peyote (Lophophora williamsii) stated, "The greatest of the Kiowa gods is the sun . . . . while the peyote (button), with its circular disk and its bright center, surrounded by white spots or rays, is its vegetal representative." At another point Mooney remarked, "Briefly stated, it may be said that the Indians regard the **mescal** as a panacea in medicine, a source of inspiration, and the key which opens to them all the glories of another world." In addition to its ritual use, its medicinal values are by no means neglected. "The Indians frequently use the **mescal** in decoction, without any ritual, for fevers, headaches, and breast pains . . . I have also seen an Indian eat one between meals as a sort of tonic appetizer'."[8]

The epidemic proportions of narcotic addiction in a city as large as Chicago and its attendant crimes and arrests have made it possible to investigate the nature of addiction along multi-disciplin-

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ary lines.* A study of the external conditions of life of the addict through an epidemiological approach, and a study of the internal (intrapsychic) conditions of life through interview, and therapeutic or clinical psychological techniques have made it possible to approach this subject in a holistic manner. This "in vivo" study included the comparison of addicts who were actively on drugs and addicts who had recently withdrawn from drugs. Most studies of the effects of drugs have been done in controlled laboratory settings.[9] While this "in vitro" approach has the advantage of maintaning a constant environment and thereby controlling a key variable, it deprives one of observing clearly the reactions of subjects in their natural habitat. It, of course, becomes crucial to evaluate this key variable. In this article, the material reported is limited to an investigation of the intrapsychic life of the addict. The epidemiology of addiction is being reported elsewhere.

St. Marks Church* until recently ran a program for the rehabilitation of drug addicts. In the course of evaluating their mental status, psychological tests including the Rorschach, Thematic Apperception Test, Projective Drawings, and an abbreviated Wechsler Adult Intelligence Scale were administered. The same tests were administered to a group of drug addicts in Cook County Jail. All of those in the St. Mark's population reported on here were actively addicted and had taken their last shot at least 15 hours before the evaluation. Those in Cook County Jail had been withdrawn from drugs for at least one month. The two groups of twenty were comparable in age. The average age was twenty-nine with a standard deviation of 1.5, the range being 18 to 35 for both groups. The amount of school completed was 10 grades on the average with a standard deviation of 2.0. All of those tested for intelligence fell within the normal range with intelligence quotients from 90 to 110; the average was 103. Their socio-economic background was similar enough (i.e., . . . they all came from high census tract drug addict areas and were similar in race, income, etc.) to assume no variation in this respect of the base.

The results of testing revealed a high degree of aggressivity in the incarcerated non-actively addicted group in contrast to the non-incarcerated actively addicted group (hereafter referred to as Group I and Group II respectively). It should be noted that the autocratic jail setting might tend to encourage aggressive behavior; however, the low level of aggressivity of persons actively on drugs strongly suggests that taking the drug diminishes aggressive feelings. Note that the term "taking the drug" is used, rather than the term "the drug" itself. It is common knowledge, even amongst the addicts themselves, that there is relatively little pure heroin in their package. Thus the term "taking the drug" relates to the whole process of obtaining it, the ritual of its administration, and in the subsequent semi-sleep state. The needle, the drug and all of the artifacts in this process may become conditioned stimuli for escape activity. In this instance, escape means retreating from reality in much the same manner as the catatonic patient does. We know, for example, that the addict begins to feel relief and satisfaction after he has achieved the money to buy the drug, often long before he injects it into himself. Language itself may also serve to trigger off certain conditioned responses. In group discussions in the jail, weaving, nodding, itching, and even nausea were not uncommon symptoms directly associated with talk about drug taking. This was especially true if the special argot of the addict was employed. That this tended to disappear after a time attests only to the phenomenon of extinction (the verbal stimuli did not receive reinforcement from actual experience). Several men, just prior to discharge from Cook County Jail, demonstrated withdrawal symptoms common to the "cold turkey" withdrawal of an addict actively on drugs. This occurred even

*Initially under the auspices of the Department of Neurology and Psychiatry, Northwestern University Medical School.

*This aspect of the program was carried out in conjunction with the Reverend Robert Jenks' Counseling Center at 4427 S. Drexel, Chicago, Ill.

with some men who were away from drugs for a year or more. Again a pattern of conditioning is suggested. We can speculate that the conditioned stimulus was an unpredictable and undependable environment—as they perceive the world outside the jail. This is the very same stimulus that is in general associated with the precipitation of addiction. The addict literally runs for the needle whenever the stress for him becomes overwhelming. This approach finds support in Hinkle's recent findings. He stated: ". . . the evidence from these studies also indicates that although man is surrounded throughout his life by a host of potential 'causative' agents of disease and carries with him always his genetic susceptabilities, he develops illness most frequently at times when he is having difficulty adapting to his environment."[11]

The same test material revealed a higher degree of depression in Group II than in Group I. This is contrary to common sense expectation which would lead us to conclude that those on drugs would be relatively free of depression and those in jail would, because of their daily life, be more deeply depressed. There is a possible explanation for this phenomenon. Those in Group II were free of the anxieties associated with being arrested. They were assured of their meals and lodgings. They did not have to concern themselves with acquiring the drug, hiding from friends and family, and the law. This is in contrast to the ultra-segregation of the addict within a ghettoed area. While Group I was somewhat isolated in jail by the administration and non-addict inmates, there were often many of them housed together in such a manner that the jail could provide a cohesiveness and a feeling of not being alone that was common to the addict in the street. A "non-active addict" is more likely to trust others and to make friends than his actively addicted peer.

The group in jail, however, when they looked back on their past experiences while on drugs, rarely reported the heightened depression so observable in those on drugs. While they clearly noted the pain of withdrawal and their general conditions of life, for the most part being "high" with heroin was associated with a pleasant state. One can speculate that this type of denial of past pain occurred because of a principle of hedonism as related to memory or perhaps the addict recalled only his very early experiences with drugs. There was a sharp contradiction between the actual mental state of the actively addicted subject as seen through clinical psychological evaluation and verbal accounts of "non-active addicts" regarding this period.

The finding that at least certain addicts actively on drugs were depressed goes counter to much of the literature on this subject, of which the following is an example:

> "The pleasure which morphine induces in susceptible individuals is one of the most subtle and enjoyable sensations known to man. . . . Actually, morphine produces a sensation of pleasant relaxation, ease, and warmth. It resembles the feeling one gains after working in the garden or completing some other pleasant task. In this state, all worries vanish and the individual can sit and dream deferring all decisions until tomorrow. One should keep in mind that in taking drugs to induce this state, the addict is seeking the same thing we all desire—peace and comfort."[10]

The above rather widely held view would seem to apply more to the early stages of addiction and/or to re-addiction. Although it has been factually demonstrated, more research is needed in order to investigate the etiology of depression as a consequence of prolonged addiction.

The relative absence of clinical psychological indications of aggression and the heightened depression in Group II and its converse in Group I strongly suggests a relationship between these two components. It is not fully clear whether or not one can ascribe this shift solely to drug use; however, the appearance of minimal aggressivity and maximal depression on the one hand and maximal aggressivity and minimal de-

pression on the other hand in a comparable group in a better than chance fashion does suggest a functional relationship between these two components. Piotrowski's[12] approach to percept analysis of Rorschach responses provides a valuable lead in an attempt to explain the above. The animal movement responses on the Rorschach test are assumed to be based on roles and modes of behavior learned early in life. The movements may involve flexor or extensor activities, or they may be blocked. Thus an "animal climbing," or "running" would involve extensor movement. As such, it is thought to reflect assertive activity. Juxtaproposed to this would be the flexor movements, i.e. . . . sitting, kneeling, bending, which in turn are assumed to reflect passive-submissive roles. The human movement responses are assumed to reflect more recently learned roles. A predominance of human movement over animal movement responses occurs with maturation. Few human movement responses, if any, are seen in young children whose primary associations involve percepts of animals.

In both Group I and Group II those responses that reflect the early adaptive pattern of the individual reveal a predominance of passive responses. In the actively addicted group, there were extremely few human movement responses or responses reflecting more recently learned patterns of behavior. In the non-actively addicted group, human movement responses were mainly aggressive —i.e., . . . "people fighting," "hitting," "arguing." Thus, one can conclude that the early life pattern of both groups, as reflected on the Rorschach were the same, but that drug use has possibly wiped out, or erased temporarily the more recently acquired patterns of behavior. Heroin then would appear to act, at least in part, as an inhibiting agent to those cortical activities which have to do with more recently acquired adaptive functions.

In relating the bodily and behavioral components of aggressivity-passivity, Wolff[13] remarked: " . . . Darwin points out that the dog, meeting an enemy, walks upright on extended legs, with tail high and stiff. In contrast, when meeting its master, the body sinks downward or even crouches and is thrown into flexing movements, so clearly expressive of affection, of the least direct service to the animal. They are explicable solely as expressions of the complete antithesis of the attitude and movements which are assumed when the animal intends to fight. *Equally striking is the contrast between the indignant and the submissive man.*" (Italics ours).

One of the very striking differences observed between the active and non-active drug user in this study was the upright, outgoing extensor posture and movements of the non-active addict and the bent, crouching, withdrawing posture and movement of the active drug user.

In studying the organism in motion, there was convincing evidence that heroin use (in a selected group of addicts) tended to diminish an area of consciousness through direct interference with cortical activity. That the same phenomena can occur with little or no drugs (the needle and certain words becoming the conditioned stimuli) attests to conditioned reflex activity that probably develops along operant lines.

Many other dimensions of personality were similarly studied. Similarly, differences between the actively addicted and non-actively addicted persons were observed in other dimensions of personality as were the verbal reports of feelings of the latter while on drugs. As interesting as any single finding is the one involving the methodology, which provided for a study of a particular disease entity in motion, was the most rewarding.

The appearance of different qualities of mental life and the contradictory nature between current ideation and previous affect reveals some of the complexities of mental functioning in the addicted as well as the non-addicted person. Most of all, it reaffirms the ancient adage of Heraclitus that "The same man never steps foot into the same river."

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CLINICAL PATHOLOGICAL CONFERENCE*†

DR. L. CARDON, Chairman

DR. I. DAVIDSOHN, Secretary

Admission: This 57 year old white female was admitted because of sharp, intermittent pain in the right upper quadrant of her abdomen. The pain had started suddenly one week prior to admission, shortly after ingestion of a heavy, fatty meal. Since that attack, she had several episodes of similar right upper quadrant abdominal pain radiating to the back and right inguinal region, and two episodes of chills with fever up to 101°. For the 2-3 days prior to admission, she had also had repeated profuse, watery diarrhea. The patient denied nausea but had several episodes of emesis.

For the past ten years she had experienced bloating and eructation after meals. There was no history of intolerance to fried or fatty foods, jaundice, alcoholism, or weight loss.

The remaining history included the usual childhood diseases, occasional frontal headaches, mild exertional dyspnea and right renal calculus associated with urinary tract infection, treated conservatively. For the past 20 years she had hypertension treated with medication unknown to her. The patient's mother and sister have diabetes melitus.

Physical Examination revealed a middle-aged, markedly obese female in no acute distress. The speech was thick. Examination of the head, ears, nose and throat showed no abnormalities. The pupils were not remarkable; the sclerae were white; the eye grounds were not examined. The trachea was in the midline; the thyroid was normal; the neck veins were not engorged. The lymph nodes showed no enlargement, and the skin was warm and moist. The chest was symmetrical with equal excursions bilaterally. The lungs were clear to percussion and auscultation, and the breasts were pendulous with no palpable masses.

Blood pressure: 170/100. Pulse: 70 and regular. Temperature: 98.3°. Respirations: 20. The heart was not enlarged, and there were no thrills, murmurs or rubs. A_2 was louder than P_2. The abdomen was markedly obese with active bowel sounds and marked right upper quadrant tenderness. Muscle guarding was noted over the entire abdomen, and no organs could be palpated. A Murphy tap on the right side gave an equivocal result. The genitalia were found normal. A rectal examination was not done. The neurological examination was negative.

Hospital Course: Initially, the patient was placed on a "medical liquid" diet, given Meperidine for pain and Methylisoctenylamine (Octin) 1^0 mg. i.m.; the latter drug was given daily throughout the whole hospitalization. Penicillin (600,000u.i.m.) was also given daily, and Sodium Nembutal was used for sedation.

On the day following admission, the patient was still complaining of the above described abdominal pain. She appeared confused, and complained of nausea and abdominal distention. The body temperature was normal and remained so all the time. The abdomen now appeared distended and tympanitic; the RUQ tenderness was unchanged with the addition of some rigidity and a palpable mass in this area. A levine tube was inserted with continuous suction and intravenous fluids were started: 1000 cc. of 5% glucose in saline with added vitamins, followed by 1000 cc. of glucose in water with 20 mEq of KCl. Suction through the Levine tube yielded 200 cc. of fluid.

On September 18 numerous skin lesions were noted around the lips, which lesions consisted of blisters on an erythematus base and were suggestive of herpes simplex. "Red patches," about 2 cm. in diameter, appeared scattered on the forehead. The patient complained of

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* Presented on Friday, April 3, 1959, 11:00 A.M.

† From the Department of Pathology of The Chicago Medical School and the Mount Sinai Hospital, Chicago, Illinois.

paresthesias of lower extremities and there was questionable pedal edema and slight puffiness around the eyes. She also complained of generalized itching and pain in the small joints of hands. Examination of the abdomen showed no change. At this time, Promazine hydrochloride was added as symptomatic treatment and, in view of the oliguria (about 30 cc. for the past 24 hours) a Foley catheter was inserted. A single dose of 100 mg. Hydro-cortisone was added to the intravenous fluid consisting of 1500 cc. of 5% glucose in water with ascorbic acid.

On September 19th, the patient appeared lethargic and critically ill. Although the lungs were clear to percussion and auscultation, there was evidently some difficulty in respiration. Blood pressure was 200/100. The oliguria persisted: 30 cc./24 hrs. Intravenous fluid therapy was continued with 1000 cc. of 5% glucose in water with vitamins and 500 mg. of Tetracycline b.i.d. which was subsequently added daily to i.v. fluid. Sustagen through a Levine tube was used for internal feeding. In view of the marked acidosis, 1/6 Molar Sodium Lactate (1000 cc.) was given intravenously.

At this time, the patient was seen by a consultant, who in addition to the above physical findings noted a huge, tender, cystic mass in the RUQ, definite right costovertebral tenderness, hematuria, pyuria, numerous glitter cells in the urine, rare narrow casts, isosthenuria, profound oliguria and progressive hypertension with normal eye grounds. Pelvic and rectal examinations at this time were normal; there was some dullness and diminished breath sounds and crepitant rales over the right pulmonary base posteriorly.

The following day (Sept. 21), the consultant noted edema of the skin of the dependent lateral abdominal wall and thighs. He described the RUQ mass as "having assumed the feel of matted loops of bowel and high pitched tinkles, rushes and a splash sound could be elicited." On his advice, flat X-ray of the abdomen was performed revealing a gas distended large intestine and 2-3 shadows in the RUQ suggestive of gall stones. In addition there was found another shadow of calcium density in the pelvis, suggestive of possible fibroid tumor of the uterus.

The patient's condition showed no change on September 20th; she was still lethargic. Pulse was 70 and regular and blood pressure 200/110. The urinary output showed some improvement (122 cc/24 hrs.) Intravenous treatment was continued, but Penicillin was replaced by Penicillin-Streptomycin combination (Dicrysticin, 1 amp. daily i.m.). In addition, Kantrex (250 mg.) was given i.m. every 12 hours. The following day, the patient showed some improvement and was more responsive. The bowel sounds were extremely hypo-active; blood pressure was 190/70, pulse 72. There was no pericardial friction rub or uremic frost. Total output now was 230 cc. in the past 24 hours. Regular insulin (15 u.) was added to the i.v. fluids as well as Sodium bicarbonate.

The urinary output was improving, and on September 23rd the patient passed 627 cc./24 hrs. The abdomen appeared softer, bowel sounds were louder and the general condition better. Intravenous fluids were continued, a total of 1500 cc. per day including 500 cc. of 1/6 Molar lactate. Regular insulin was increased to 25 u. daily and given hypodermically.

In spite of the improved urinary output (last three days: 570 cc., 330 cc., 160 cc.) the patient's condition showed a down-hill course; she became restless and had to be restrained. Her face became covered with uremic frost and on September 25th Kussmaul breathing appeared. The patient perspired profusely and was in semi-coma. She expired at 2:45 A.M.

Chairman Cardon: The meeting will come to order.

Dr. Mandel, will you discuss the protocol, please?

Dr. E. Mandel: It is a privilege to try to discuss the diagnostic possibilities of this case which is quite challenging because this middle-aged lady was apparently well until a short time before she came to the hospital and died approximately a week after the onset of her

TABLE I
LABORATORY RESULTS

Date	Hemo	Hemat.	RBC	WBC	Polys	Stabs.	Lymphs.	Mon.	Proth. T.	Sed. Rate
9/17/58	12.6	42		14200	70	15	8	7		47
9/18									17"	
9/20	12.6	39		38800	89	5	3			
9/23	11.6		3.5	34000	93	2	2			

Blood Chemistry

Date	Gluc.	BUN	CO_2	K	Cl	Na	Serology	Creatinine	Serum pH
9/17	83	129					Neg.	10.1	
9/18		95	14		85			11.6	
9/19			11	5.7	77	121			7.28
9/20		133	16	5.6	78	114			
9/24		140	17	6.6	66	122		11.0	7.31

Urine

Date	Glucose	Sp.G.	Prot.	WBC	RBC	Casts	Culture
9/17	Neg.	1.010	1.5 gm.	Many	Many		
9/19							E. Coli
9/20	Neg.			Many	Many		
9/24	Neg.		Trace	Occ.	Few		

Date	Bilir. Tot.	Bilir. Dir.	Thymol Turb.	Ceph. Flocc.	Alb.	Glob.	Alk.* Phos.	BSP** 45%	C-Reactive Pr.	Chol L.E. Prep.
9/17	0.9	0.65	1.9							
9/18				1+	2.3	3.2	12.1		3+	
9/20										299 Neg.

Blood culture: 9/20 and 9/22: Neg.
ECG: 9/17: abnormal, non-specific.
9/25: 24 hrs. urine for protein - 2.0 gm.

* Bodansky units
**45 min. retention

illness. Although the admitting diagnosis was that of an acute gallbladder attack, it was eventually shown that she had uremia and was much sicker than she had seemed to be at first.

This 57-year-old white female was admitted because of sharp, intermittent pain in the right upper abdominal quadrant. The pain had started suddenly one week prior to admission, one hour after the ingestion of a heavy "fatty" meal which, according to the chart, included a buttered steak sandwich. Since that time, she had experienced several episodes of similar abdominal pain, which radiated to the back and right inguinal region.

Thus far, this sounds like biliary colic, but why should pain which is due to biliary colic radiate to the inguinal region? This is quite uncommon, though I assume it can happen; as a rule, radiation of gallbladder pain is upward rather than downward.

This, and a number of other findings which we are going to consider presently, may lead us to suspect that perhaps even these episodes had something to do with the right kidney rather than with the gallbladder.

There were two episodes of chills with fever up to 101° F. For two to three days prior to admission, the patient also had profuse watery diarrhea, a symptom which I find difficult to explain. It may have to do with the azotemia which she apparetnly already had at that time, resulting in uremic colitis. However, the chart fails to mention any diarrhea during her hospitalization.

The patient denied nausea, but had had several episodes of emesis during the week preceding admission. For the past ten years, she had had similar attacks of right upper quadrant pain and also experienced bloating and eructation after meals. This part of the history would seem to compel us to conclude that she did have gallbladder disease, probably complicated by gallstones. Whether or not this lesion was the primary disease at the time of admission, however, is another question.

There was a history of mild exertional dyspnea and a right renal calculus associated with urinary tract infection in the past, both of which were treated conservatively. Here we have the first definite evidence in the history that she had previous kidney disease. We do not know whether on admission the calculus was still there, or had been passed; nor do we know whether she had persistent or recurrent pyelonephritis, at least on the right side.

For the past twenty years she had had hypertension, and was treated with white pills, the nature of which she did not know. This may be related to the above-mentioned frontal headaches, but we can only speculate on these points.

The patient's mother and sister had diabetes mellitus, but the patient herself apparently did not. There is only one blood glucose finding in the chart—80 mg/100 ml—which is normal. This, of course, does not necessarily exclude the possibility that she did not also have mild diabetes.

Physical examination revealed a middle-aged, markedly obese female, in no acute distress. The fact that she was over forty, obese, and a multipara may add some support to the diagnosis of gallstones. Her speech was thick, perhaps due to the uremia which will be discussed more fully later, and also to some dehydration which may have been present. Examination of head, eyes, ears, nose and throat showed no abnormalities. The pupils showed no change from the normal: the sclerae were white. She obviously was not jaundiced. The eye grounds were not examined for reasons which are not stated. The trachea, thyroid, neck veins, and lymph nodes also showed no changes from the normal.

The skin was warm and moist. The chest was symmetrical, with equal excursions bilaterally. The lungs were clear to percussion and auscultation. The breasts were pendulous and no palpable masses were present.

The blood pressure was 170/100, and subsequently ranged around 200/100 until the very end, indicating a persistence of her hypertension. She did not have any episode of hypotension during the course of hospitalization. The pulse was

regular and, indeed, remained normal throughout. Respirations were 20 per minute. Examination of the heart revealed no abnormality; the abdomen revealed marked obesity, with active bowel sounds and marked upper quadrant tenderness. Muscle guarding was noted over the entire abdomen, but was apparently more prominent over the right upper quadrant. As may be expected with such an abdomen, no organs could be palpated.

These findings are compatible with chronic and perhaps recurrently active cholecystitis, possibly also cholangitis. The attending physicians considered the diagnosis of cholecystitis and cholangitis, and the possibility of gallbladder empyema was entertained.

Looking over the laboratory results, we find that, on the day of admittance, she had a practically normal hemoglobin and hematocrit. The red cell count was not depressed until some days later, at which time it was 3.5 million, while the hematocrit and hemoglobin remained within the normal range. The white cell count was elevated to 14,000, with some left shift; the serum urea nitrogen was 129 and creatinine 11.6 mg/100 ml. Thus the finding of marked azotemia, in the face of the above-mentioned diagnoses, evidently came as a surprise.

One or two days after admission, serum chlorides were found to be only 85 milli-equivalents; CO_2 was 14—only half the normal value, and serum pH was low, indicating a significant metabolic acidosis.

The urine, according to the chart, was muddy in appearance and loaded with both red and white cells. There was considerable proteinuria and the urine exhibited a low specific gravity. The total serum bilirubin and thymol turbidity were normal, and the cephalin flocculation test was negative, but the serum alkaline phosphatase was elevated to 12 units.

Dr. Kirshen: The direct serum bilirubin was not normal because you have a value of 0.65.

Dr. Mandel: I agree. The direct serum bilirubin was slightly elevated, even though the total was normal.

The B.S.P. was 45 per cent. These results certainly are consistent with gallbladder disease. Whether there was an increase in the total serum bilirubin subsequently is not apparent either from the clinical description or from available laboratory findings. The alkaline phosphatase, of course, should always be considered in the light of at least two organ systems, the hepatobiliary tract and the skeletal system. In view of the fact that she had advanced renal insufficiency as evidenced by the presence of metabolic acidosis and an increased urea nitrogen and creatinine, the possibility of either primary or secondary hyperparathyroidism must be considered. Perhaps I will have a chance to come back to this point. Together with the marked B.S.P. retention, the serum alkaline phosphatase elevation certainly fits the diagnosis of hepatobiliary tract disease. Whether the abnormal laboratory results may, in part, be attributed to some hepatic congestion cannot be ruled out.

Blood cultures were negative, even though there was evidence of very severe infection, as indicated by white blood counts of 38,000 and 34,000 a few days after admission in spite of the absence of fever.

At this point, I may say that the patient most probably had chronic cholecystitis and cholelithiasis, but I do not believe these conditions caused her acute and fulminating disease and final demise.

Briefly reviewing her course in the hospital, we note that nausea, abdominal pain and distention persisted in spite of medication with analgesic and spasmolytic drugs. The right upper quadrant tenderness remained unchanged, but some additional rigidity and a palpable mass in this area was noticed. This could, of course, be gallbladder empyema or hydrops; or one might consider it to be an enlarged pyelonephritic kidney, although subsequently we note that a consultant regarded the mass as possibly representing matted bowel. Treatment now included Levine Tube with continuous suction and intravenous fluids.

On September 18th, two days after admission, skin lesions around the lips were noted consisting of blisters on an erythematous base. I am not sure I can fit this clearly into the over-all picture. It is quite possible that this was a herpes simplex infection. At one time, the suggestion was made in the chart that the entire symptomatology may have had to do with disseminated lupus, including this rash. But I cannot see much evidence in favor of this diagnosis.

The patient complained of paresthesias of the lower extremities, and there was questionable pedal edema and slight puffiness around her eyes. She thus was apparently not excreting the same amount of fluids as she received in her veins. Hence, she subsequently developed more edema.

Another complaint was noted, that of generalized itching. This may be attributed to the uremia; it was treated with Promazine.

The patient became severely oliguric, indeed almost anuric, in spite of the use of a Foley catheter, and appeared lethargic and critically ill. Although the patient's lungs were reported to be clear to percussion and auscultation, there was evidently some difficulty in respiration which may be attributed to incipient pulmonary congestion or edema.

At this time, patient was seen by a consultant, who, in addition to the above physical findings, noted a huge, tender, cystic mass in the right upper quadrant, definite right costovertebral tenderness, hematuria, pyuria, numerous glitter cells in the urine, rare, narrow casts, isosthenuria, profound oliguria and "progressive hypertension, with normal eye grounds."

The latter findings, together with the severe azotemia and the practically normal hemoglobin, indicate to us that this woman had not been suffering from renal insufficiency for a long period of time. Rather, she had a fairly acute type of uremia, even though we know she has had some renal disease and obstructive ureteropathy on the right side in the past.

The consultant also found dullness, diminished breath sounds and crepitant rales over the right pulmonary base posteriorly, presumably broncho-pneumonia.

In order to investigate the right upper quadrant mass, which felt like "matted loops of bowel," an x-ray of the abdomen was taken, which revealed a gas-distended large intestine and dense shadows in R.U.Q., suggestive of gallstones, and another shadow in the pelvis, interpreted as possibly representing a fibroid tumor of the uterus or a stone in the bladder.

I wonder, Mr. Chairman, if we may ask Dr. Nadelhaft to show the x-rays at this point.

Chairman Cardon: All right; we can do that.

Dr. Nadelhaft: We have only two films of the abdomen of this patient, and this is the best one (Fig. 1). It shows a suction tube in the stomach; this tube happens to point at these three calcified upper right quadrant stones which have the characteristic appearance of gallstones.

We can make out neither kidney shadow, and there is no evidence of the calcified stone that was mentioned previously as having been found in the right kidney.



FIG. 1. Scout film of abdomen, demonstrating gall stones and calcified uterine myoma.

The colon is moderately distended with gas, but there is no evidence of small bowel distention. In the pelvis, there is a shadow, three centimeters in diameter, which has the appearance of calcification in a leiomyoma of the uterus.

Dr. Kirshen: Isn't that a mass close to the spinal column?

Dr. Nadelhaft: Yes.

Dr. Kirshen: Is that not the kidney, or at least, where a normal kidney would be?

Dr. Nadelhaft: Well, it could be. I don't think we have enough evidence on the basis of one film to make a definite statement. There could be a mass behind here; but it wouldn't be lying correctly for the kidney. I mean, it is just a possibility, but we do not have further films to confirm it.

Dr. Kirshen: Actually it would go out to the lateral abdominal wall, which was more of what was present on the physical.

Dr. Nadelhaft: Yes; I see.

Dr. Mandel: Can you see the left kidney?

Dr. Nadelhaft: No; we cannot see the left kidney. We can see the psoas margin here, but not on the right side.

Dr. Mandel: You cannot make out either kidney clearly?

Dr. Nadelhaft: That is correct. I can see the psoas margin on the left side, but I cannot see it on the right side. So, it is possible that this is a large renal mass. We do not have any chest films to document any of the possible lung changes which may be caused by uremia.

So, what we have are gallstones, probably a calcified uterine fibroid, and, as has been pointed out by Dr. Kirshen, the possibility of an enlarged kidney on the right.

Chairman Cardon: Thank you, Dr. Nadelhaft.

Dr. Mandel: The patient continued to go downhill, although there seemed to be some improvement for one or two days, with increase in urinary output. She had Kussmaul breathing, continued to have severe metabolic acidosis and progressive increase in azotemia to about 130 or 140 BUN, and developed uremic frost.

In spite of all therapeutic measures, she expired.

I would attribute her death to renal insufficiency or, perhaps, better expressed, to uremic potassium intoxication, along with bacterial intoxication. She had both fulminating infection and severe renal insufficiency.

Now, if I may try to detail for a few minutes what her problems seemed to be, I would list them as follows:

1. She had gallbladder disease. There can hardly be any question about it in view of the history of attacks of pain, the digestive symptoms, the x-ray findings and the increase in serum alkaline phosphatase and direct bilirubin.

What speaks against this gallbladder disease's playing a major role in the final illness is the absence of significant jaundice, and the overwhelming renal impairment.

2. She obviously had renal disease:

a) chronic renal disease, in view of the history of calculus and infection. However, I do not believe that she had enough chronic renal disease to cause renal insufficiency and azotemia because of what I mentioned before—absence of significant anemia and of eye ground changes. In other words, she may have lived a sort of borderline existence in terms of the number of functioning nephra available, until finally something happened, either an obstruction again, or an ascending or hematogenous infection which caused an extremely severe and acute pyelonephritis, possibly pyonephrosis, at least on the right side. What one would have to postulate, then, is that the left kidney, though infected, continued to produce urine. Perhaps the right kidney was blocked for a long time by a calculus, or else there was no longer a calculus, but pyelonephritis was rampant in both kidneys.

It is somewhat unusual to see death within a few days as a result of acute pyelonephritis. One would have to postulate an extremely virulent micro-organism. And it is not only infection that this patient had, but also severe and acute renal insufficiency. It is particu-

larly the renal insufficiency that I am referring to which is an unusual sequela of acute pyelonephritis.

One of the possible complications I was considering is papillary necrosis. This woman, even though she had no diabetes, did have obstructive ureteropathy and, therefore, possibly papillary necrosis, one of the recognized fatal complications of pyelonephritis.

b) The possibility of a malformation is to be considered, including horseshoe kidney, polycystic disease, hypoplasia, and agenesis. In other words, if this patient had only one functioning kidney, or a limited portion of one kidney making urine, the rapidly advancing azotemia precipitated by acute pyelonephritis can be more readily understood.

c) Among the other complicating factors to be considered, I should mention an accelerated phase of hypertension. This woman had hypertension for a long time, and she now had severe uremia. This type of hypertension may sometimes take a very short course of only a few weeks.

However, the absence of eye ground changes, in addition to the absence of a characteristic urinary sediment, speaks against it. Of course, she might have had pyelonephritis plus malignant hypertension. Then the urinary sediment, packed with cells, would not allow us to distinguish casts of various types, particularly broad casts and red cell casts. However, the observed blood pressure readings were not high enough to make malignant hypertension a good choice.

d) A fourth diagnosis that I might mention briefly, and which is also mentioned in the chart, is acute tubular ischemic necrosis or lower nephron nephrosis—possibly secondary to acute gallbladder disease, or some GI disease such as perforation of a viscus, or localized peritonitis. It is the oliguria, of course, which might lead one to suspect the possibility of lower nephron nephrosis. However, there is no evidence of any episode of hypotension, and, again, the urine microscopic picture is not in favor of this lesion.

e) One might further consider interference with renal circulation by, for instance, an embolus or thrombus, which put one kidney out of commission while the other succumbed to the active infectious process. This, I cannot rule out entirely.

I think this takes care of most of the diagnostic possibilities that one might mention all based on the concept that acute pyelonephritis alone is unlikely to lead, in so short a time, to renal insufficiency and fatal uremia.

I should like to say a word about the hypertension related in the history. It is possible, of course, that it might be due to the chronic pyelonephritis. However, as far as I recall, hypertension due to pyelonephritis develops only when there is sufficient azotemia, in other words, when there is marked renal insufficiency due to the pyelonephritis. This, I think, I have ruled out, on the basis of absence of eye ground changes and of significant anemia.

The hypertension might be attributed to unilateral renal disease—that is, pyelonephritis and/or renal ischemia on one side, and a fairly normal kidney on the other, in order words, a "Goldblatt" kidney. Again, the absence of eye ground changes would tend to rule out significant hypertension of long duration.

I mentioned the possibility of either primary or secondary hyperparathyroidism before. The primary disease may be considered in connection with the calculus, but there is no good evidence otherwise. A secondary hyperparathyroidism would deserve consideration only if we believe that this woman had long-standing renal insufficiency, which, indeed, I do not.

In summary, I submit that this patient had (1) gallbladder disease, chronic, not significantly contributing to the terminal, fatal illness; (2) she had pyelonephritis, both chronic and acute, possible pyonephrosis—all this complicated by either papillary necrosis, or a developmental anomaly; and (3) her past hypertension was of the "essential" type, not directly or causally related to her renal disease.

Dr. Kirshen: It was stated that this patient was not diabetic, yet she was

given insulin. Could you explain that, please?

Chairman Cardon: She was given insulin because of the hyperkalemia, I believe, Doctor.

My impression of the case when I first saw the patient is best summarized in the consultation note which I wrote at the time, from which I will take the privilege of reading:

"The history of renal calculus and urinary infection in the past, the onset of the present illness with fever, chills, R.U.Q. pain (radiating to the groin) and tenderness, nausea, vomiting, the findings of a huge, tender, cystic mass in the R.U.Q., right costovertebral tenderness, hematuria, pyuria, numerous glitter cells, rare casts (not broad), isosthenuria, leuckocytosis, profound oliguria, and progressive hypertension with normal eye grounds would all seem to be compatible with a primary surgical (right sided) renal disease such as pyelonephritis or pyonephrosis (related or not to urinary calculi) with secondary diffuse, bilateral pyelonephritis.

Another aspect of the matter which cannot be minimized is the clinical impression of acute cholecystitis by the attending physician at the onset of illness. On this basis the cystic mass in the R.U.Q. would be a huge hydrops or empyema of the gallbladder and the normal temperature now due to control by antibiotics. The elevated B.S.P. and serum alkaline phosphatase could go along with this (although the cephalin flocculation and thymol turbidity and bilirubin tests are normal); and the renal findings of oliguria and uremia then would be on the basis of lower nephron nephrosis and/or the so-called hepato-renal syndrome. If calculi are present the possibility of an underlying hyperparathyroidism must be remotely considered.

It is noted that 24 hour urinary output two days ago was **30 cc.** and yesterday **200 cc.** with diminution in redness and turbidity; serum K^+ is 5.6 meq.; and serum CO_2 and pH have responded somewhat to 1/6 M. Na^+lactate I.V.; serum Na^+ and Cl^- remain low; serum urea N has not risen above 129 mgs.% as yet."

A regime of treatment was outlined as for lower nephron nephrosis or acute renal shutdown from any cause, with special emphasis on restriction of combined oral and parenteral fluid intake to an amount equal to the previous 24 hour urinary output plus the estimated insensible loss. Achromycin 500 mgs. b.i.d. was added to the I.V. fluids. We considthe advisability of transferring this patient to an institution with an artificial kidney and instituting dialysis. However because of the spontaneous rise in the 24 hour output from 30 cc. to 200 cc. in the two days, with diminuation in redness and turbidity of the urine, it was decided to wait and watch developments. In the following two days the 24 hour urinary output increased to 432 cc. and then to 627 cc., and our conservative policy seemed to be paying off.

When this diuresis occurred, then, we of course, relinquished any idea of artificial dialysis, because it seemed as if it was not necessary and the prognosis was better.

We thought perhaps we were dealing with a reversible lower nephron nephrosis, or an acute pyelonephritis or pyonephrosis which was subsiding under therapy with antibiotics, and that the patient would now get along very well. Then the output went to 570 cc. to 330 cc., and finally to 160 cc., during the 24 hours before her death. But even then you will see that it was much more than the 30 cc. which we had to consider originally.

Therefore, rather than consider the artificial kidney we relied on what you read—insulin, glucose, and saline, which she was getting for other reasons also; but predominantly and mainly we treated her with the potassium-free resin—the resin No. 48, made by Smith-Klein and French, which is an ammonium-hydrogen cycle resin, not containing potassium—which, theoretically, removes potassium from the bowel and causes a reversal of flow from the blood to the bowel and thus to the outside.

I saw the patient again on 9/21/58 at

which time the following comments were made:

> "The patient's condition remains unimproved; there is edema of the skin of the lateral abdominal wall and thigh indicating that the amount of I.V. fluid cannot be increased."

We had been tempted to increase the intravenous fluids as diuresis began in the hope of diminishing the azotemia more rapidly.

> "The WBC has risen to 38,000, and the neutrophils to 88%. The mass in the R.U.Q. has now assumed the feel of matted loops of bowel; there are high-pitched tinkles and peristaltic rushes, and a splash sound can be elicited."

These new findings were interpreted to mean that there were now superimposed loops of dilated (reflex ileus? local peritonitis?) bowel, overlying and perhaps adherent to the infective mass which we had originally felt in the R.U.Q. A flat x-ray of the abdomen was advised as was surgical consultation.

Now Dr. Feinhandler has come in again. Would you take a few minutes to discuss your case?

Dr. Emanuel Feinhandler: Well, I think after this excellent discussion by Dr. Mandel there is very little I can add except that nobody can know the type of patient that you have from reading a history.

The first time I saw this patient was just about a week before she was admitted to this hospital. She came in with a typical history of a cholecystitis which was proven by a Graham Cole Test in the office.

The next time she called for help the clinical picture was again the same—pain in the upper right quadrant, vomiting and marked tenderness plus a palpable liver.

Now, on that basis, plus the fact that her temperature prior to admission was over 102, she was admitted with a diagnosis of acute cholecystitis, and possible empyema of the gall bladder.

After this, from the history, you can see the picture was entirely different, and I am sure the post-mortem findings will also be quite interesting.

Chairman Cardon: I think it is only right to point out that Dr. Feinhandler, in his evaluation of the case at the house, had no inkling that there was uremia present at the time.

Are you raising your hand, Dr. Greene?

Dr. Earle Greene: Yes.

From a surgical point of view, here is a woman who unquestionably had gall stones, kidney pathology, and perhaps also hypertension.

Her given age was 57. I am wondering what her physiological age was. I would be a lot happier if she was 20 years older, because I have on several occasions seen a rutured appendix in elderly people do exactly what has happened to this woman. I therefore suggest as a possible diagnosis a ruptured appendix which aggravated all of her previous diseases.

Chairman Cardon: Dr. Kirshen.

Dr. Kirshen: Apart from the preponderance of the kidney disease in this patient, we cannot get away from the history—and the history is typical for acute gall bladder disease.

Whether the patient was in uremia before or not, we do not know. Naturally it is very difficult if you do not see a patient and do not examine him; you have to rely on different opinions and different findings; but a very good possibility, instead of assuming a ruptured appendix, would be a ruptured gall bladder with a covered peritonitis—with a peritonitis being localized and producing this mass which then was palpated by the consultant.

Chairman Cardon: I think we will defer any further discussion until after the pathological findings, to give Dr. Davidsohn an opportunity.

Dr. Greene: Just one word—the ruptured appendix in elderly people is a relatively bland disease. A ruptured gall bladder is a terrific disease that cannot compare with the blandness that we have here.

Chairman Cardon: Dr. Davidsohn.

Dr. I. Davidsohn: To begin with, the patient had gall stones—several of them. They were quite sizeable. But the gall bladder wall showed no significant re-

cent changes. It was thin, and the mucosa was quite delicate.

The basic lesion was in the right kidney. The kidney was soft and mushy, with pus flowing out from various places, producing an abscess in the vicinity and infiltrating the perirenal fat tissue.

It weighed 560 grams. A normal kidney weighs about 150 Gm.

The kidney pelvis was dilated.

The urinary bladder showed petechial hemorrhages.

A probe inserted into the distal orifice of the right ureter was stopped by a stricture 2 cm. above the orifice.

Proximal to the stricture the ureter was dilated and contained two impacted stones, one about 5 x 2 millimeters, the other about half that size.

The proximal portion of the ureter was dilated and its wall hypertrophied. The kidney pelvis was also dilated. (Figs. 2, 3, 4)

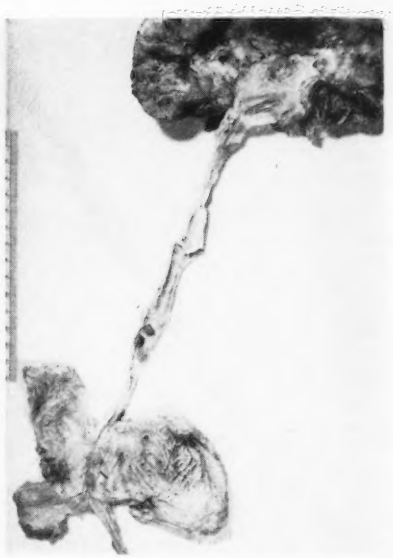


FIG. 2. Right kidney, and ureter, and segment of left ureter. Urinary bladder. Two calculi impacted in the right ureter.

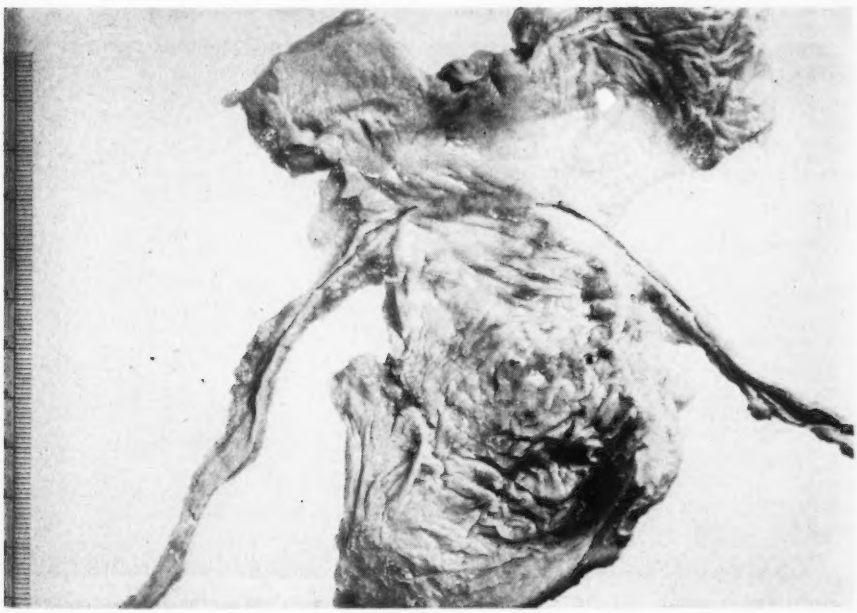


Fig. 3

Close-up of distal portions of both ureters and urinary bladder. The trigone is smooth and lacks the normal configuration.



FIG. 4. Close-up of right ureter showing impaction of the calculi, the dilatation of the lumen and the thickening of the wall of the ureter proximally to the impacted stones.

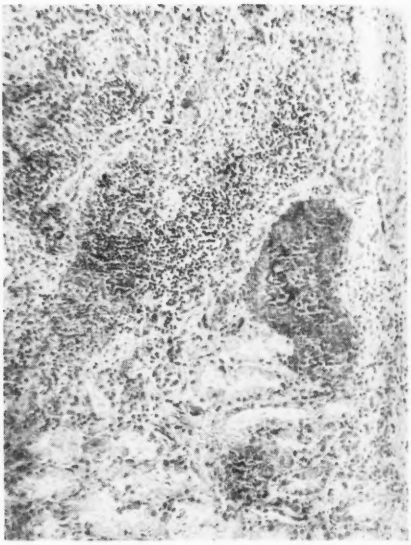


FIG. 6. Right kidney. Acute suppurative pyelonephritis with multiple abscesses and extensive destruction of parenchyma. 65X.

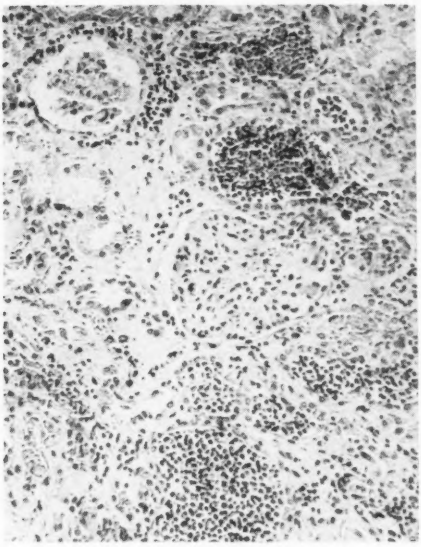


FIG. 5. Right kidney. Acute suppurative pyelonephritis showing accumulations of thick leukocytic exudate in the tubules, some of them widely distended. 100X.

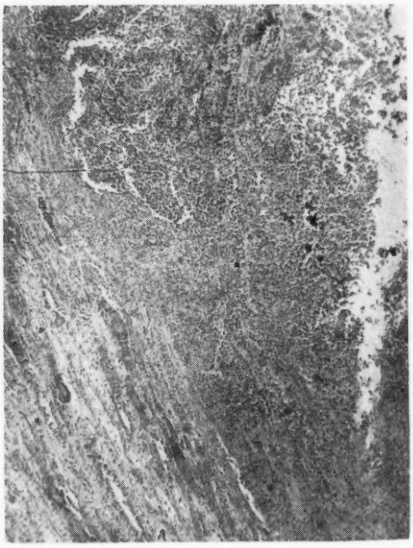


FIG. 7. Right kidney. Acute suppurative pyelonephritis. Large abscess in region of papilla. 25X.



FIG. 8. Right kidney. Acute suppurative pyelonephritis. Pus in collecting tubules. 25X.

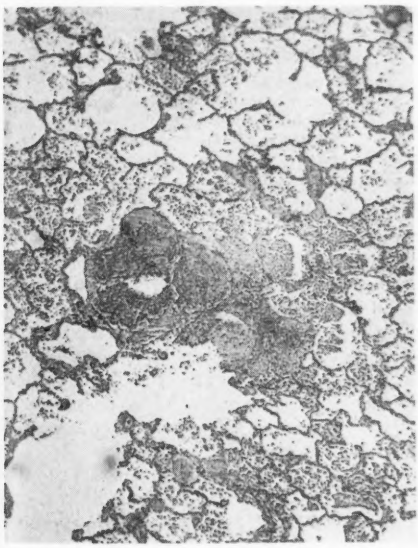


FIG. 9. Lung. Acute necrotizing pneumonitis, focal, uremic. 25X.

Histologic examination showed acute suppurative pyelonephritis.

The glomeruli were only slightly affected. Many tubules were distended with pus. Some glomeruli were enlarged and showed slight early acute changes, an acute glomerulitis. (Fig. 5)



FIG. 10. Uterus. Calcified submucus fibromyoma. Section surface. X-ray picture of myoma on left.

Small abscesses were present with resulting destruction of the kidney substance, but even in these areas the glomeruli were well preserved. Chronic changes were minimal, possibly obscured by the diffuse suppuration.

The same type of lesion was present in the pyramids; the tubules were filled with purulent exudate. (Figs. 6, 7, 8)

Very little functioning renal parenchyma was present.

The process extended into the papillae.

The mucosa of the renal pelvis showed chronic pyelitis.

The arteriols showed only slight sclerotic changes. The lumens were not significantly narrowed, which is interesting in view of the history of hypertension.

It is apparent from these changes that the function of this kidney was seriously impaired.

The left kidney was absent: renal agenesis. The left ureter was present for a distance of 12 centimeters.

The trigone in the urinary bladder was malformed, a finding well known in the

urologic literature on unilateral renal agenesis. Accordingly, if one finds, in the course of cystoscopic examination, only one functional ureteral orifice, and a malformed trigone, the diagnosis of an absent kidney can be made.

As is usual in such cases, only the right renal artery was present; the left was absent; also, only the right renal vein was present; the left was absent.

The lungs were large and heavy, with extensive pulmonary edema. In one area, and only in one of several slides examined, there was early necrosis of the pulmonary tissue: uremic pneumonitis. (Fig. 9)

The paucity of this lesion suggests that it was recent, as was the uremia.

The calcification shown by Dr. Nadelhaft in the x-ray picture was a submucous, calcified, fibromyoma of the uterus. An x-ray picture of the uterus and the appearance of the section surface confirmed that calcification was present. (Figs. 10, 11)

Dr. Zimmerman: What is that in the lower left, in the cervix?

Dr. Davidsohn: This is a cyst, a cystic erosion.

In summary:

ANATOMIC DIAGNOSIS
A-188-58

Kidneys:
Right:
Hypertrophy (560 Gm.)
Acute suppurative pyelonephritis.
Ureteral calculi and stricture.
Chronic pyelitis.
Left:
Agenesia.
Absent left renal artery.

Urinary Bladder:
Petechial hemorrhages.

Heart:
Hypertrophy
Coronary arteries: slight arteriosclerosis.

Lungs:
Pulmonary edema.
Focal pneumonitis (uremic?)

Gallbladder:
Cholelithiasis

Uterus:
Intramural and submucous, calcified fibromyoma (3.5 cm.)
Acites (400 ml.)

Cause of Death:
Acute suppurative pyelonephritis of solitary right kidney.
Congenital absence of left kidney.
Renal failure.

Dr. Cardon: Very good.

Dr. Zimmerman: What did the liver show?

Dr. Davidsohn: No significant changes. It was a little heavier than normal. It weighed almost 2,000 grams.

The usual periportal infiltrates were present as seen in patients with gallstones.

Dr. Zimemrman: Did it show the periportal infiltrates throughout?

Dr. Davidsohn: That's right.

Dr. Zimmerman: There were no stones along the biliary tree?

Dr. Davidsohn: None were recorded, Dr. Zimmerman.

Chairman Cardon: Dr. Maslow.

Dr. Maslow: Sometimes an unusual formation of the ears is pointed out as an indication of a congenital anomaly of the kidney. Was there any such malformation here?

Dr. Davidsohn: The condition that you are referring to is characterized by the presence of depressed tip of the nose, by large prominent ears, and by an epicanthus. These charges were described by Dr. Edith Potter in renal agenesis in the newborn.

It was not present in this case. It is my impression that these facial changes are seen mainly in the newborn and in young children and in cases in which the lesion is probably not compatible with long life.

Chairman Cardon: Dr. Maslow is in a hurry to leave, apparently, and we saw here that there was a stricture of the ureter and some calculi.

We must remember that at the time we saw the patient, the patient was in deep uremia. I wonder if Dr. Maslow would like to talk about how he would have handled this case.

Dr. Maslow: Before this case was shown by the pathologist I wanted to ask a question.

My question is, what objection was there to passing a catheter to the right kidney in view of the fact that the patient very definitely was in uremia?

From the history and physical examination of this patient, we knew that she had pathology of the right kidney. We had no direct evidence as to the condition of the left kidney, but, because of the presence of uremia, we could surmise that something was abnormal about the left kidney or else it would have compensated for the diseased right kidney and uremia would not have developed.

In such a case, where there is a possibility of pathology of both kidneys, there is an urgent need to rule out possible obstructive uropathy. We have a standing rule that whenever you have a patient with anuria and developing uremia, even when the symptoms and signs point to a medical nephritis, one should do a flat plate of the abdomen to rule out nephrolithiasis. One should pass ureteral catheters and even do retrograde pyelography if it seems indicated for establishing a diagnosis. I have done these procedures on many occasions in cooperation with medical men on the assumption that it can do the patient no harm and the information obtained may be life saving.

Apropos of the "gall bladder disease syndrome" presented by this patient, it is a fairly common occurrence for patients to be admitted to the hospital with a diagnosis of gall bladder disease only to discover that the "gall bladder dis-



Fig. 11. X-ray picture of myoma.

case syndrome" was really a uremic manifestation as proven by the presence of marked azotemia.

Chairman Cardon: Dr. Maslow, two questions.

Would you have passed a catheter on a patient in uremia with a 30 cc. output even though both kidneys are present?

Number two—assuming you did, and you found a stricture and stones, with the patient in this condition what would your future course have been?

Dr. Maslow: The answer to the first question is definitely "yes." This is even more urgent when the patient has only one functioning kidney.

The answer to the second question, namely if you find a stricture and stone in the ureter of the solitary kidney and the patient is in uremia—the immediate indication is to perform an emergency cystoscopy and attempt to pass a ureteral catheter by the stricture and stone and into the renal pelvis. I would desperately try to accomplish this, because if you are successful the kidney begins to secrete urine immediately in the majority of cases. The battle is won. The patient soon develops compensatory diuresis and the medical man has but to stand by and guard against electrolyte imbalance. The patient is well in a matter of days and you can then plan and treat surgically the underlying pathology at your leisure.

If you are not successful in passing a ureteral catheter you must immediately perform an emergency nephrostomy.

The earlier these measures are employed the better the prognosis. You are dealing with a desparately sick patient and these measures are life saving. Therefore, these steps should be taken without delay. You have nothing to lose and a great deal to gain.

Chairman Cardon: Thank you very much. Dr. Mandel, do you have anything further to say? I think you should be congratulated on a beautiful analysis and certainly a very close shot at the diagnosis.

Dr. Mandel: I would like to question, again, the congestion of the liver. I am still puzzled about the high alkaline phosphatase.

Chairman Cardon: That is directed to you, Dr. Davidsohn. Was there any congestion of the liver to explain the B.S.P. retention and the high alkaline phosphatase?

Dr. Davidsohn: There was nothing unusual, Dr. Mandel, in the microscopic examination, except what one finds in a patient with a systemic infection and gallstones.

Dr. Mandel: Could there have been congestion?

Dr. Davidsohn: Yes, moderate congestion was present.

Dr. Zimmerman: I am also disappointed in what the liver doesn't show. It is unusual to have 45% B.S.P. retention and not have a tangible reason for it. Heart failure and various space-occupying lesions of the liver as well as intrinsic liver disease could give B.S.P. retention to this degree. With so high an alkaline phosphatase level, space occupying lesions such as metastatic carcinoma come to mind.

None of these things were shown here, and I do not know what is the explanation. Fever certainly was not high enough to cause this level of B.S.P. retention, and this degree of B.S.P. retention would be rather unusual as being due to fever. In malaria we have seen levels of 25 per cent B.S.P. retention, with return to normal within 24 or 48 hours after the temperature returned to normal. So, this is a very puzzling problem.

I frankly had expected lesions of roughly the following variety: I thought this patient might have a gallstone in one hepatic duct. This can give you an elevated alkaline phosphatase, but a normal bilirubin level. This has been shown in dogs: if you ligate one hepatic duct the serum alkaline phosphatase values goes up sharply, but the serum bilirubin level remains normal. Even this, however, would not explain the B.S.P. retention.

One possibility was multiple portal abscesses due to incomplete obstruction; there were not there. I do not know what the explanation is.

I am making these comments because I would not want the impression left

that the B.S.P., or any liver test, is so capricious that it would be so abnormal without any reason. There are reasons for most abnormalities, and this is one of the exceptions.

Chairman Cardon: This is an exception, and you have no means of explaining it at all.

Dr. Davidsohn: What would you expect to see? Would you expect an ascending cholangitis?

Dr. Zimmerman: An ascending cholangitis would certainly explain it.

Dr. Davidsohn: That was not present. Cloudy swelling was present as one sees in a patient of this type. In the sections I examined, and in the gross description there were none of the changes that were mentioned by Dr. Zimmerman.

Would you say that this patient's renal failure had no bearing on hepatic function?

Dr. Zimmerman: Well, we have had some opportunity to study this. We have studied B.S.P. retention in patients with terminal uremia from chronic nephritis and other types of renal insufficiencies. B.S.P. retention to the degree seen here is generally related to the kinds of renal insufficiency that are also related to hepatic disease, such as carbon-tetrachloride poisoning, etc.

Chairman Cardon: What about an oliguria? Would you think that that would have anything to do with this aside from the uremia?

Dr. Zimmerman: Well, as you know, about 80 per cent of a dose of B.S.P. is removed from the blood by the liver and then excreted through the duodenal tree; the remaining 20 per cent is removed, even in the hepatectomized animal, by some other (?RE) system. B.S.P. does appear in the urine, but the amounts in the urine are only noticeable when there is an impairment of biliary excretion. It is not an important amount, and if you nephrectomize an animal you can still clear the blood quite well of B.S.P. I therefore do not think that the oliguria has much to do with this.

Dr. Davidsohn: I have several questions. Would you consider one test, particularly if done only once, sufficient to draw conclusions?

Dr. Zimmerman: No. I think it would be very easy to dismiss it and say it could be an error.

The interesting thing is that most errors in doing B.S.P. give you very high levels, probably because one of the sources of error is using the same syringe to draw the blood that has been used for the dye. Rarely does drawing blood from the same vein when there has been a little extravascular spread of the dye cause falsely high values although this is something the patient would notice quite promptly. So, this result could be an error. I am just surprised to see an alkaline phosphatase level of 12 and a B.S.P. retention of 45%, and I have been laboring for an explanation.

Chairman Cardon: I will call on those that wish to further discuss the case in the order in which I saw their hands. Dr. Maslow, please; you had your hand up.

Dr. Maslow: I was just reminded that six weeks ago we had a woman come in with anuria. We knew that she had a nephrectomy four or five years ago. We passed a catheter up to the remaining kidney and we got urine; she then developed a diuresis that was due to the dislodging of a stone at the renal part of the junction. Then, after that, we operated on her, although she had only one kidney, and removed the stone. She made an uneventful recovery and she went home.

The reason for the urgency of the operation was even more than if she had two kidneys. If that happened again, and if she couldn't get any help quickly, something fatal might happen to her.

Chairman Cardon: Dr. Greene.

Dr. Greene: Dr. Davidsohn, can you account for the mass they felt in her right upper quadrant?

Dr. Davidsohn: Yes, a huge kidney, about four times the normal size.

Dr. Greene: Was it that big?

Dr. Davidsohn: Yes, 560 grams, as compared with about 150 of the normal size.

Chairman Cardon: Do you want to say something, Dr. Zimmerman?

Dr. Zimmerman: The possibility that this was a case of multiple gallstones is another consideration, or, of course, both tests may have been in error, B.S.P. and alkaline phosphatase. This is somewhat unlikely.

If there were only B.S.P. or alkaline phosphatase abnormality, one might feel freer to dismiss the result as only a laboratory measure. But with several indications pointing to hepato-biliary disease, I'm disappointed that we cannot prove it.

With reference to another facet which has already received comment, I would like to mention briefly two mistakes that we made, within the same week, when I was visiting on the service at the R and E Hospital several years ago. In both instances we thought we felt a markedly enlarged spleen, and in both instances the mass represented pyelonephrosis with a markedly enlarged kidney. This should not be a common error, but it is quite understandable now that we have seen it.

Chairman Cardon: I have seen a patient with a huge hypernephroma of the kidney who was sent to the office by the referring physician with a diagnosis of splenomegaly; and, indeed, it felt like a spleen except that it was always palpable in the costovertebral angle, and the pyelogram showed it was a huge kidney.

Dr. Davidsohn: I would like to make a remark about Dr. Zimmerman's previous statement.

It is quite possible, of course, that a small stone in one of the ducts was overlooked. Our sectioning of the liver would not necessarily discover all of the ductal stones within it.

Dr. Zimmerman: As a matter of fact, in fairness to the Pathology Department, I think that when you are about to have a post-mortem examination done on a patient who has gallstones, you ought to add a note to the chart, or call the Pathology Department and ask them to particularly look for intraparahepatic calculi. They are described in the literature much less frequently than I think they occur.

Chairman Cardon: Dr. Mandel.

Dr. Mandel: They had discovered still another liver test that was abnormal. The prothrombin time was 17.

Dr. Davidsohn: What is our normal prothrombin time?

Dr. Mandel: Twelve to thirteen.

Chairman Cardon: Dr. Greene.

Dr. Greene: I think in many instances, perhaps in most instances, where a stone has passed through the common duct into the duodenum, it is common enough to see evidence of it in an enlargement of the cystic duct, and perhaps enlargement of the diameter of the common duct.

Now, I wondered about hepatic stones. A patient might possibly pass stones through the common duct that would, perhaps, be lost in the liver proper. There, of course, you must get a history of severe attacks of colic; however, the stones that form primarily in the substance in the liver itself are almost always pigment stones. They are not mixed stones.

I think if you get a pigment stone you can say that this probably formed in the liver proper and did not form in the gall bladder.

Dr. Zimmerman: This would make sense. I was not attempting to suggest formation in the liver necessarily, but I did want to suggest the possibility of a gallstone passing into the biliary tree, and then for one reason or another entering the hepatic duct.

Was the cystic duct enlarged, Dr. Davidsohn?

Dr. Davidsohn: Yes, it was enlarged. I would like to say something else here.

We are apparently attaching much importance to the value of a test. I think this is correct. But I think that one should not do it unless one does the next thing: whenever one finds an abnormal test, one should have it repeated.

For example, take the figure of the prothrombin test, 17, compared with a normal of 13. Can you draw conclusions from that unless it was found more than once?

The same applies to any of the other tests. Considering many tests which are done and found to be completely normal it would seem justified that if you

have an abnormal finding to have the test repeated.

Chairman Cardon: I think we all agree and have stressed again and again that abnormal tests should be repeated. However there never was any question, in my mind at least, that we were dealing primarily with a renal problem here. Because of the numerous venipunctures which were necessary here both for diagnosis and treatment, it was essential that the veins be preserved as much as possible. The patient's veins were becoming very bad, and, therefore, only the most necessary venipunctures were ordered.

If I may close with a few remarks, I think of this whole discussion, the thought that is most important for us to carry away is Dr. Maslow's statement. It was my impression—and perhaps that is the reason we did not suggest G.U. consultation—that in the presence of marked oliguria and severe uremia the passage of a catheter carried a certain amount of risk in that it might accentuate or produce a complete anuria reflexly, and that a urologist would refuse to do it.

Of course, on reflection, it is apparent that we did not always have this fear. I refer particularly to the anurias due to sulfanilamid concretions, in which the routine treatment was the passage of ureteral catheters. I recall cases in which on cystoscopy, sulfa concretions were seen protruding from the ureteral orifices in the bladder. When these concretions were grasped by forceps and removed, and ureteral catheters passed, urine immediately began to flow, the uremia disappeared, and the patient recovered. I think then, that in the future, we should all remember to ask for the urologist's help in every case of anuria or uremia, even if the condition appears to be entirely medical in nature.

I would like to comment on Dr. Mandel's statement about uremia in acute pyelonephritis. I have had a case of this type in a man with chronic leukemia, who acutely developed fever, chills, sweats, pyuria, hematuria, cylindruria and severe uremia. On appropriate antibiotic therapy the pyuria and uremia cleared up rapidly and the patient recovered.

As far as the differential diagnosis between gall-bladder and renal disease in this case, there are several points that deserve emphasis. The fact that the abdominal pain radiated into the groin is very significant. I have not seen gall bladder pain radiate to the groin; whereas, this radiation is characteristic of renal or ureteral disease. The tenderness in the right costo-vertebral angle also points toward renal disease. The history of ureteral calculi and urinary infection in the past was extremely important. To summarize, then, the radiation to the groin of the R.U.Q. pain, the costo-vertebral tenderness, the pyuria, the 38,000 WBC and neutrphilia, and the past history of calculi and urinary infecton left no question at all that renal infection existed. The only question was, was there associated gall bladder disease or not?

It may not be out of place here to stress the fact that a single significant physical finding (e.g. spider nevi) may be as important or more so than any liver function test in calling attention to liver disease. Similarly in other diseases the proper interpretation of historical data and physical findings may be paramount in the correct diagnosis.

Now a word or two about the diagnosis of a tender mass in the R.U.Q. in a special situation, namely, congestive heart failure. During episodes of heart failure a large tender liver in the R.U.Q. occurs almost as a rule. The reverse is, however, not necessarily true; that is, not every large tender mass in the R.U.Q., even in the presence of heart failure, is necessarily a passively congested liver even though this diagnosis is often assumed categorically. We have seen several cases of this type; two were acute empyema of the gall bladder, and one turned out quite unexpectedly to be a large pyonephrotic sac of the right kidney. In all of these cases the mass had been mistakenly assumed to be a tender congested liver because of the presence of congestive heart failure.

In our case the autopsy showed that the large tender mass on the right side

of the abdomen was the single compensatorily-hypertrophied right kidney, with the complicating infection.

And one question—were the parathyroids examined?

Dr. Davidsohn: Yes. The parathyroids were slightly enlarged. They were weighed, however, after having been in formalin, so I am a little concerned whether the weight that we got can be correctly interpreted. The weight was about 500 milligrams—larger than the size indicated.

I would like to comment on Dr. Greene's question with regard to the mass on the right side. Please note that not only was the kidney large, but there was also a perinephritis; there was an inflammation of the fat tissue due to a ruptured abscess of the kidney. That no doubt added to the bulk of the mass.

Dr. Feinhandler, do you have anything else to add?

Dr. Feinhandler: No.

Chairman Cardon: The meeting is adjourned.



ERRATA

The following references were omitted from the Abstract Section of Volume 20, Number 3, September 1959.

West, M. and Zimmerman, H. J.: Serum Enzymes in Disease I. Lactic Dehydrogenase Activity and Glutamic Oxaloacetic Transaminase in Carcinoma. A.M.A. Arch. Int. Med. *102*:443, 1958.

Zimmerman, H. J., West, M. and Heller, P.: Serum Enzymes in Disease II. Lactic Dehydrogenase and Glutamic Oxaloacetic Transaminase in Anemia. A.M.A. Arch. Int. Med. *102*:115, 1958.

West, M., Heller, P. and Zimmerman, H. J.: Serum Enzymes in Disease III. Lactic Dehydrogenase and Gltamic Oxaloacetic Transaminase in Patients with Leukemia and Lymphoma. Am. J. Med. Sci. *235*:689, 1958.

West, M. and Zimmerman, H. J.: Serum Enzymes in Disease IV. Lactic Dehydrogenase and Glutamic Oxaloacetic Transaminase Levels in Renal Disease. J. Lab. and Clin. Med. *52*:185, 1958.

BOOK REVIEWS

CARE OF THE SURGICAL PATIENT, by Jacob A. Glassman, M.D., F.A.C.S., F.I.C.S. and Raymond W. McNealy, M.D., F.A.C.S., F.I.C.S. The Williams & Wilkins Company, Baltimore, 1959. 320 pages.

These two authors, both of whom have wide clinical experience, have written a book which should have wide appeal to the medical student, house officer, resident in surgery and practicing physician. They have attempted, in outline form, to bring order to a field which is growing at such a fast rate that even those who have made it their life's avocation often find it difficult to keep up with.

Because of its format, the book tends to be dogmatic in style, but the authors are quick to point out that the successful practice of modern day surgery calls for much besides technical dexterity, and that nothing can replace the thoughtful evaluation of any given problem and a decision to action based on individualized treatment rather than blind adherence to empiric routine.

Each page and chapter is full of useful information which is presented in an extremely logical fashion. It is for this reason that it has great appeal as a book to keep handy whenever one is dealing with a surgical patient. Great emphasis is placed on the meticulous details of pre- and post-operative care which are often left to an interne or resident who may be all too unsure of himself with regard to matters which may later prove critical.

Among the interesting chapters are the following: Psychosomatic Considerations in Surgical Care, Steroids in General Surgery, The Cardiac Surgical Patient, The Pregnant Surgical Patient, Hospital Infections, Cardiac Arrest, Pre- and Post-Operative Infant Feeding, etc.

There are no references but rather ample room for notes by the reader. This book is not a text book of surgery, and the authors did not intend it to be thought of as such. Instead, it is a reminder of some of the various aspects of good surgical practice which are so vitally necessary for the well-being of the surgical patient and which may be forgotten in the rush to wield a knife.

* * * *

PYELONEPHRITIS. Fletcher H. Colby, M.D. The Williams & Wilkins Company, Baltimore, 1959. 214 pages.

Only within recent years has the problem of pyelonephritis been recognized as being so serious. This clinical problem is seen in all of the specialty fields of the practice of medicine.

In this book, presented mainly in the interest of the medical student and general practitioners, the embryology, anatomy and physiology of the kidney are first thoroughly reviewed. The incidence, etiology, symptoms, diagnosis and treatment of both acute and chronic pyelonephritis are discussed with emphasis on early vigorous treatment of the acute stage so that the chronic form, which is often symptom free and very difficult to successfully treat, may never be reached.

Separate chapters are devoted to the problem of pyelonephritis in childhood, diabetes and pregnancy. Again a separate chapter is devoted to the problem of hypertension and pyelonephritis.

Numerous case histories, taken from the wealth of pathology as seen in the Massachusetts General Hospital supplement the subject matter. Many excellent x-rays are also included so that the reader may view the cases in much the same manner as does the urologist.

N.G.

* * * *

BIGGER'S HANDBOOK OF BACTERIOLOGY. F. S. Stewart, M.D. (Dublin), F.R.C.P.I. The Williams & Wilkins Company, Baltimore, 1959. 602 pages and 92 illustrations.

This book is an attempt on the part of the author to give to the medical student and the General Practitioner a "shorter" textbook of bacteriology. It is not intended to replace the more detailed works in the field. It discusses, in textbook form, General Properties of Bacteria, Cultivation of Bacteria, Disinfection and Sterilization, Antigen-Antibody Reactions, Immunity and Hypersensitivity, Classification of Bacteria, Viruses, Rickettsia and Bacteriophages.

As intended, this book is necessarily brief, omits theoretical considerations whenever possible, and does not dwell on details primarily of interest to the bacteriologist. If supplemented by adequate lectures and a comprehensive laboratory manual, this book may prove sufficient for the beginning student. Parasitology and Mycology are not considered in the text and this necessitates other books for the student.

The interested student who wishes a more comprehensive study of any particular subject will find this book inadequate and, should he wish to look elsewhere, will find the lack of a bibliography an omission on the part of the author.

The use of the title "Handbook" is unfortunate since it implies to the student that it is a review book. The student, studying for Board examinations, wishes an outlined, factual, and complete review of a subject and will find this book unwieldly for such purposes.

The General Practitioner will probably wish to refer to more complete discussions of his particular problem rather than to a short survey text.

This book, a somewhat abbreviated version of the standard texts, cannot be recommended to the advanced student or to the inquiring clinician. It may be valuable to the beginning medical student as the basis for further reading.

R.W.S.

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